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DESIGNER DRUGS

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DESIGNER DRUGS

THURSDAY, JULY 18, 1985

U.S. SENATE,
COMMITTEE ON THE BUDGET,
Washington, DC.

The committee met, pursuant to notice, beginning at 9:10 a.m., in room SD-138, Senate Office Building, Hon. Lawton Chiles, presiding.

Present: Senator Chiles.

OPENING STATEMENT OF SENATOR CHILES

Senator CHILES. We will call our hearing to order.

The nation's drug profile has changed dramatically over the years. In addition to the continuing importation of large quantities of cocaine, heroin and marijuana into this country, the United States has become a source country for the production of domestically grown marijuana. We have also seen the diversion of prescription drugs into illicit markets and the clandestine manufacture of various controlled substances such as PCP, LSD, and methamphetamines. The health consequences and enforcement costs as the United States continually changes its response to the drug abuse problem have far-reaching budget implications.

A vivid example of the forces in action within the illicit drug market was produced by the clandestine manufacture and distribution of PCP. During the decade of the 1970's, the hallucinogenic drug PCP began to appear in the Los Angeles area and quickly became of serious concern to the community, local law enforcement, and health professionals. Initially, PCP was mostly a California drug abuse phenomenon and Los Angeles was known as the PCP capital of the Nation. The Los Angeles Police Department and Los Angeles County Sheriff's Department considered the PCP problem more significant than either heroin or cocaine. PCP then began to spread. Today it is a major problem throughout the country and especially here in the Nation's Capital.

PCP and the circumstances surrounding its emergence as a nationwide problem indicates to many that our national drug law enforcement and medical communities were taken by surprise and were not equipped to respond to a serious emerging drug problem, even though the source was within our national boundaries. In the case of PCP, California provided an early warning of a new drug consumption and production trend that could have been used by law enforcement and medical officials to develop an effective countermeasure before the use of PCP spread to other parts of the

Nation. However, no one at the Federal level seems to have been listening or able to act decisively.

DESIGNER DRUGS ARE EXTREMELY DANGEROUS

Today, another new development in drug trafficking is occurring predominately on the west coast; the production and use of dangerous substances known as designer drugs. Last March I brought the designer drugs problem to the attention of my colleagues. These synthetically manufactured drugs present some of the same issues that PCP presented in the early 1970's. As in the case of PCP, our national drug strategy may not be adequate to detect and respond to the emerging designer drugs problem. Here I think we have an opportunity to try to get ahead of the wave.

Designer drugs are extremely dangerous from a health standpoint. The drugs are thousands of times more potent than the illegal narcotics presently flooding the country, and over a hundred deaths have been identified with designer drugs use so far. Furthermore, these drugs have been responsible for causing long term neurodegenerative diseases in some users. The human and medical economic costs of designer drugs are potentially devastating.

Law enforcement efforts against designer drugs have been limited. According to DEA, only four clandestine designer drugs laboratories have been immobilized in this country, one in October 1984 in Brownsville, TX; one in April 1985 in San Diego; and two in June 1985 in North and West Hollywood, CA.

The designer drug phenomenon could revolutionize the way drugs are used and sold in this country. Designer drugs are manufactured in clandestine laboratories by phantom chemists. The cost of manufacturing designer drugs is only a fraction of the cost of smuggling heroin or cocaine into this country, and the profits to be realized are much greater. Consequently, the potential exists for organized crime, which controls the heroin and cocaine markets, to enter into the designer drugs area, in both the production and distribution ends.

PROBLEM MUST BE DEALT WITH

The purpose of this hearing is to determine what is known regarding designer drugs, the nature and extent of the problem, and to identify what countermeasures this Nation should take now and in the future to combat the spread of designer drugs. In responding to designer drugs, this Nation is not dependent upon other countries. We can act decisively within our own boundaries to deal with this emerging problem. We plan to explore the potential benefits that a coordinated and integrated approach and partnership between the law enforcement community, medical community, education sector, and private industry might bring to the problem.

How should the Federal Government deal with the designer drug problem? Can the Federal Government provide the leadership and act as the catalyst to formulate a timely and comprehensive response to the designer drugs problem?

I particularly want to express appreciation to Mr. and Mrs. Kidston who will share with us some of their tragic family experience. I hope what they can tell us will provide information and understanding to trigger action on the designer drug problem and also cause a fear of the use of these drugs.

We are delighted to have Senator Cranston to introduce our California witnesses.

Senator, we are delighted to have you here. I can tell you that the witnesses that come to us from California are the people literally that discovered the problem, who coined the phrase, who understand more about this problem and can help us at the Federal level shed light on it.

We are delighted to have you here to introduce this panel. We know of your long work in this field and how interested you have been in trying to stop the flow of drugs in this country.

Senator CRANSTON. Thank you very much, Mr. Chairman. I applaud your leadership in taking steps that should enable us to come to grips with this problem. I am delighted to introduce three experts in the field of designer drugs. These individuals are from California and unfortunately that gives them particularly keen insight into this subject since the deadly synthetic drugs are largely manufactured and distributed in my home State.

Dr. J. William Langston is Chairman of the Neurology Department at Santa Clara Valley Medical Center and also assistant professor of neurology at Stanford University. He was instrumental in determining the connection between MPPP and the premature onset of Parkinson's disease. Dr. Langston appears to be in the forefront of the devastating problem.

Dr. Gary Henderson is an associate professor of pharmacology and toxicology at the University of California at Davis. Dr. Henderson is credited with coining the phrase "designer drugs." He presently operates one of the few labs in the country devoted to a class of designer drugs, fentanyl analogs, which are many times more potent than heroin.

Mr. Randy Rossi is a Special Agent and Law Enforcement Legislative Advocate with the California Department of Justice and Bureau of Narcotics Enforcement. Mr. Rossi was one of the original framers of legislation to outlaw fentanyl.

I am pleased to introduce these experts to you and I am certain that their testimony today will confirm what we have heard about the designer drug problem, that it is grave and growing and must be dealt with immediately. I will work with you, Mr. Chairman, with the committee, and with all others who are interested to see to it that we come to grips swiftly and effectively with the evil blight of designer drugs.

I thank you again for your leadership.

Senator CHILES. I thank you for your appearance and the introduction of these witnesses and the continued effort you give to us.

Now we will hear from Congressman Charles B. Rangel, who is the chairman of the House Select Committee on Narcotics Abuse and Control.

LEGISLATION INTRODUCED TO CONTAIN SPREAD OF DRUG

Earlier this year I first became aware of the designer drug problem and in March introduced legislation calling on the administration to develop a law enforcement strategy to contain the spread of designer drugs. Chairman Rangel joined me in that effort and introduced a companion bill in the House. In April Attorney General Meese said he would move expeditiously and last week the Attorney General announced legislation to give law enforcement the tools to back up the enforcement effort. I want to congratulate you for joining in this latest effort. Our paths have crossed in Latin America and Central America and many other parts of the world as your committee has brought the drug problem to our attention. I am delighted to see your efforts in this particular cause in the House. I know it will help very much.

STATEMENT OF HON. CHARLES B. RANGEL, A U.S. CONGRESSMAN FROM THE STATE OF NEW YORK

Mr. RANGEL. Thank you for giving me the opportunity to testify before the committee in which you chair and on behalf of the Congress and indeed the Nation I have to thank you for the leadership that you have shown in this area. I guess it was in 1963 when I was prosecuting drug cases and Jack Cusack, who is here with us today, was one of the narcotic agents and how we were so concerned that the Nation was not alerted to the dangers of the epidemic of heroin until it actually hit closer to home.

BUMPER CROP OF DRUGS PRODUCED

We just returned a few months ago from Vienna and the United Nations' Commission on Drugs. And they reported that every drug producer country has a bumper crop. This is substantiated by the State Department and our own committee estimated in 1984 over 10 tons of heroin have come into the United States, 85 tons of cocaine and some 15,000 tons of marijuana. As we visit our local communities we find that the law enforcement officials have all but given up in terms of believing they can control the trafficking of drugs and they are involved in what we call selective arrests because of the overcrowded court calendars and the overcrowded jails.

I guess before we get into designer drugs, it has been estimated that the industry runs well over $100 billion and if you try to even measure the loss of productivity, that is another $100 billion. So now with your leadership and what we can do in the House, we see something building up over the last few years in California. Two days ago it was reported by the Maryland State Health Department that some of the pure heroin or "China White" or designer drug has been found over there. But we do have an opportunity at least in this Congress to move and see what we can do to make certain that these chemicals are not available to our people and especially our youth. Our staff has a lot of technical data which it has shared with your committee as well as materials I am certain you have received from the Drug Enforcement Administration. While it appears to be a complex chemical matter, what is abundantly clear is that with very little money, with less than $500 in chemicals and equipment, one cup of the so-called pure heroin, "China White", could be worth on the illicit market, over $2 million, and it does not require any great skill to put together this synthetic. It can be made locally and it is a very cheap thing, an inexpensive thing to put together.

We have also been able to ascertain that it is a very dangerous drug to be used. We have a high incidence of overdoses, brain damages and other severe disabilities.

As as you pointed out, we introduced legislation to see how deep the problem is, to see how damaging the use can be and I am glad to join with you in lauding the administration for responding to our request and demanding that there be severe criminal penalties for the preparation, the use and the trafficking of these drugs. So while it is not clear as to what materials the FDA has, I am glad that your bill, S. 746, and my bill, H.R. 2014, has at least pioneered legislation in this area.

CHEMICAL MORE LETHAL THAN HEROIN

I will join with you and the respective committees to support the administration's legislation. But it is frightening to believe, and as you and I have gone into the jungles of South America and the mountains of Thailand to get some hand on heroin and cocaleaf seeds, to know that right in our own kitchens a more lethal chemical can be created to destroy the lives of our young.

Once again, you have provided leadership in the Senate, and I am proud as a House Member to join with you to see what we can do.

Thank you very much, Mr. Chairman.

Senator CHILES. I thank you so much, Chairman Rangel, for your past efforts and for your efforts in this regard. It is mind boggling to think that with all of the frustrations we are currently having in stopping cocoa, cocaine, heroin, and marijuana from coming into this country, and the amount of dollars we are spending for radar balloons, fast boats, aircraft, and personnel (including changing the Posse Comitatis Law where the military can now assist in this effort), now we have a situation where huge amounts of designer drugs can be produced in our own basements and backyards for just a few dollars. It is frustrating but with California giving us an early warning we have an opportunity to try to get out ahead of this. The legislation says it will be a 15 year offense and $250,000 fine is certainly a good start. Also, the testimony today will show how terribly dangerous it is. It is something that will give you Parkinson's disease or kill you. We need to understand, users and parents need to understand, what kind of thing we are flirting with, what kind of Frankenstein monster is being created as a result of playing with these drugs. Your help in trying to get that word out is tremendously important.

Mr. RANGEL. These hearings will go a long way to educating the American people and I ask that my full statement be included in the record.

Senator CHILES. It will be inserted in full in the record.

[The prepared statement of Congressman Rangel follows:]

TESTIMONY OF HON. CHARLES B. RANGEL, CHAIRMAN, SELECT COMMITTEE ON NARCOTICS ABUSE AND CONTROL, U.S. HOUSE OF REPRESENTATIVES

Good morning. I am pleased to have the opportunity to testify today on the problem of designer drugs. I commend the Committee for focusing on this new drug abuse phenomenon and thank you for inviting me to participate in your deliberations.

The trafficking and abuse of illicit drugs are problems of staggering proportions in the United States today. The dimensions of these problems have become all too familiar. The House Select Committee on Narcotics Abuse and Control, which I have the privilege to chair, estimates that some 10 tons of heroin, 85 tons of cocaine and 15,000 tons of marijuana were smuggled into the United States in 1984. The production of illicit drug crops abroad continues unabated, and in our own country illicit marijuana has become a major cash crop in a number of States.

Domestically, the illicit drug trade is a $110 billion a year industry. Drugs are responsible for much of the street crime that grips our nation. Although there are some signs that drug use may be leveling off, levels of drug abuse in our nation, particularly among our young people, exceed those of any other industrialized nation of the world. The social costs of drug abuse such as crime, lost productivity, and increased demand for health and social services, approach another $100 billion.

I could go on but I know the Committee is well aware of the severity of drug abuse and drug trafficking.

Now, we face a new drug threat. Although the dimensions of this problem are not yet clear, the implications of this problem are indeed frightening. At this point, the problem seems to be confined mainly to California and the west coast, but there are signs it is beginning to appear in other urban areas. Just two days ago, for example, it was reported that the Maryland State health department was issuing warnings to addicts in Baltimore to avoid a drug being sold on the streets as "pure heroin." I am talking, of course, about designer drugs.

Designer drugs are analogs, or chemical cousins, of controlled substances that are designed to produce effects similar to the controlled substances they mimick. By slightly altering the chemical formula of a controlled substance, such as by adding a floride or extra carbon molecule, a new drug is created which will produce the high or euphoria the user wants.

The crucial difference is that designer drugs are legal. The production and use of designer drugs is producing a host of public health and enforcement problems that could become much worse if effective action to control these drugs is not forthcoming.

According to information our Committee has received from the Drug Enforcement Administration, the designer drugs synthesized to date have been primarily heroin-like substances. These heroin substitutes are analogs of fentanyl (Sublimaze) and to a lesser degree, meperidine (Demerol), both schedule II narcotic analgesics. There are numerous variations of each drug that produce effects similar to heroin.

The first fentanyl analog, alpha-methylfentanyl, was encountered in California in 1979. Sold on the streets as "China White," this drug was connected to 18 overdose deaths in 1980 and 1981. The DEA placed "China White" in schedule I of the Controlled Substances Act in September 1981. Since then, however, at least six new fentanyl analogs have appeared. These designer drugs are extremely potent, some up to 5,000 times as potent as morphine. They act quickly and for a short period of time, and they have been responsible for more than 70 overdose deaths on the west coast since 1980.

An analog of meperidine, MPPP, was identified by a DEA lab in California in 1982. Careless synthesis of this drug, however, results in the formation of a highly toxic by-product known as MPTP. In California, MPTP was sold to a number of users as "new heroin," with tragic consequences. The drug produced severe brain damage with symptoms similar to the end stages of Parkinson's disease. Fortunately, "new heroin" seems to have largely disappeared since warnings of its severely disabling effects were issued.

What little we know about these heroin substitutes raises grave concerns in my mind about the potential impact of designer drugs on drug trafficking and abuse in America. The major problems, as I see them, are:

-- Designer drugs are completely legal and fall outside the regulatory framework of the Federal Controlled Substances Act and similar State laws.

-- The possible analogs of dangerous controlled substances are limitless. Designer drug chemists can create new variations faster than health and enforcement officials can identify and control them.

-- The designer drug market is not limited to heroin substitutes. Legal substitutes can be made for almost every controlled drug on the illicit market, creating a law enforcement and public health nightmare.

-- Designer drugs are produced in clandestine labs, which are hard to detect. They are subject to no quality controls on potency or purity, thus exposing users to unknown dangers.

-- Designer drugs are cheap to make and the profits to be realized enormous. It is reported that less than $500 worth of chemicals and equipment can produce a cup of "China White" worth $2 million on the illicit market.

-- Theoretically, a single clandestine lab could produce enough synthetic heroin to meet the worldwide demand for heroin-like drugs without a single opium poppy being harvested.

What can be done about designer drugs? Congress has already taken some action to address this problem. The Comprehensive Crime Control Act of 1984 (P.L. 98-473) included authority requested by the Administration to allow the Attorney General to schedule uncontrolled substances in schedule I of the Controlled Substances Act on an emergency basis if such action is necessary to avoid an imminent hazard to the public safety. Schedule I is reserved for dangerous drugs of abuse that have no legal medical use, such as heroin and marijuana. Within the past four months, DEA has used this new power to place a dangerous heroin substitute (3-methylfentanyl) in schedule I. This authority was also used to schedule the designer drug "Ecstacy" (MDMA), an amphetamine-like hallucinogen whose use has been gaining in popularity.

DEA banned the drug because research showed it may cause permanent brain damage. Action also has been taken to schedule two additional drugs, MPPP and PEPAP. Because new designer drugs can be created so rapidly, however, there are serious questions as to whether the emergency scheduling authority provided last year is adequate to control the designer drug problem.

We also need to determine the dimensions of the designer drug problem. While the problem appears to be confined mainly to the west coast at this time, a thorough assessment of the nature and extent of designer drug trafficking and abuse has not been conducted. For this reason, earlier this year I wrote to DEA, FDA and NIDA and asked them for a status report on the designer drug problem from their perspectives. Following that, I was pleased to introduce H.R. 2014 in the House of Representatives, a companion measure to S. 746 introduced by Senator Chiles. Our bills would require the new National Drug Enforcement Policy Board, established in last year's Crime Act, to provide a comprehensive assessment of the designer drug problem to Congress, along with recommendations for necessary legislation. This assessment is to be included in the Board's initial report to Congress.

I commend Senator Chiles for his leadership in introducing this legislation. Although our legislation has not been enacted, I would urge the Board to address the designer drug problem in its first report to

Congress. Certainly their report would not be complete without attention to this emerging serious problem.

Finally, we need to examine new means of regulating designer drugs. The replies I received from my inquiries to the agencies earlier this year were disheartening. The problem of designer drugs seemed to have fallen through the cracks of the bureaucracy, and there seemed to be little commitment to develop an aggressive strategy to contain the designer drug problem before it became an epidemic.

After this initial discouraging response, I was extremely pleased when the Administration submitted new legislation to the Congress about a week ago to make designer drugs illegal. The bill would establish new criminal penalties for the production and trafficking in designer drugs. Under this proposal, designer drug violations would be punishable by fines up to $250,000 and prison terms up to 15 years. I am encouraged by the Administration's action, and I believe our legislation was an important factor in making the Administration realize the depth of Congressional concern about this issue. I look forward to the opportunity to review the Administration's proposal in greater detail.

In closing, I again want to thank the Committee for your leadership in focusing public attention on the designer drug problem and for inviting me to testify on this serious issue. I am convinced that by working together we can develop the tools needed to attack the insidious traffic in these most dangerous substances.

Senator **Chiles**. Our next witness is Gary Henderson, associate professor of pharmacology and toxicology at the University of California.

Dr. Henderson, my understanding is you first coined the term "designer drugs" and I know you have one of the labs for detecting fentanyl derivatives and I know you are a recognized expert on fentanyl.

Would you please give us your testimony?

STATEMENT OF DR. GARY L. HENDERSON, ASSOCIATE PROFESSOR OF PHARMACOLOGY AND TOXICOLOGY, UNIVERSITY OF CALIFORNIA AT DAVIS

Mr. **Henderson**. I first became aware of the fentanyl problem in 1980. During 1980 there were three or four overdose deaths that occurred in southern California, These looked like typical heroin overdose cases. Autopsy reports were very consistent with heroin overdose but on chemical analysis, no drug was found at all. During that same year in California there were a number of seizures of materials that were being sold as heroin and again on chemical analysis there was no drug to be found. It took about a year for us to find out that there was a new drug being sold under the name "China White" which at that time meant very pure Southeast Asian heroin. This new drug was a relative or derivative of a drug called fentanyl. Fentanyl is probably used in 70 percent of all surgical operations in this country, if not throughout the world. Almost anyone who has had major surgery in the last 4 years has had fentanyl. It is essentially a lifesaving drug. What somebody has done is taken advantage of the fact that you can make very small alterations in the chemical structure of a drug and produce large changes in its biological activity. The new drug we found was not fentanyl but a derivative called alpha-methyl fentanyl. This was many more times more potent than heroin but it was shorter acting. It was legal for at least 2 years.

DRUG LEGAL FOR 2 YEARS

Senator **Chiles**. Legal for how long?

Mr. **Henderson**. For 2 years. There were people arrested with this material and had to be released. It was a new chemical entity.

Senator **Chiles**. You can make that, sell it, push it, use it, nothing illegal about that for 2 years?

Mr. **Henderson**. It is my understanding they even have to give the material back to you if they have seized it.

Senator **Chiles**. Yet this was many times more powerful than heroin at the time?

Mr. **Henderson**. Yes. About the time alpha-methyl fentanyl was put on the restricted drug list, a new derivative called paraflouro fentanyl came out. This was a subtle variation on the theme. Again, a very potent narcotic, completely equivalent to heroin but street legal.

Senator **Chiles**. Completely equivalent?

Mr. **Henderson**. Yes. These drugs have all of the effects of heroin.

Senator **Chiles**. They are addictive?

Mr. **Henderson**. Yes. But they are chemically different and therefore not on any national or international drug list. This new chemical eventually was put on a restricted drug list but by 1983 we had a third variation. Actually we had two variations in 1983. There were very, very subtle changes in the basic chemical structure, but then we had essentially new chemicals that have yet to be named officially.

Senator **Chiles**. And now another drug?

Mr. **Henderson**. Yes.

Senator **Chiles**. All they had to do was make some variant change and they were legal?

Mr. **Henderson**. By this time there were probably two dozen overdose deaths. In 1984 a big change occurred. We had 49 overdose cases in California in 1984 alone.

Senator **Chiles**. Those 49 cases were from designer drugs?

INCREDIBLY POTENT DRUG

Mr. **Henderson**. Fentanyl alone. I am speaking only about fentanyl. This was when the latest variant, 3-methyl fentanyl was introduced. This is an incredibly potent drug. In it is purest form it is 70,000 times more potent than morphine and 1,000 to 3,000 times more potent than heroin.

Senator **Chiles**. How many more times potent than heroin?

Mr. **Henderson**. We only have data from experimental animals, but in man it is probably 1,000 times as potent as heroin. We really don't know but we think the active dose is probably a microgram which is about the smallest amount of material you can see with the naked eye. It is an incredibly potent narcotic. This drug was made originally by a drug company in Belgium called Janssen Pharmaceutica. They have made over 200, possibly 400 variations of fentanyl. We know there are probably 400 derivatives of fentanyl that are extremely potent narcotics.

Senator **Chiles**. Any of those 400 would be legal until they are scheduled?

Mr. **Henderson**. Yes. If you really sat down and worked it, you could come up with hundreds, if not thousands of derivatives of one basic molecule. They all will be equivalent to heroin. They have all of the side effects and toxic effects. They kill just like heroin by suppressing respiration. People stop breathing, go into a coma and die. They produce the same euphoria, the same rush, that heroin does.

In fact, the 3-methyl variation may produce an even more intense rush. I think 3-methyl is 1,000 times more potent and has the same duration as heroin. It is very cheap to make and relatively easy to make. To date we have recorded 100 overdose cases in California and all associated with fentanyl derivatives. We have recently analyzed urines from individuals in drug treatment programs, methadone clinics, probation programs. In 10 percent of the urines we analyzed we found fentanyl. So we know it is being used.

Senator **Chiles**. That has got to be a pretty broad use if you are finding it——

Mr. **Henderson**. That is about the normal positive rate you find in urine screening programs. Ten percent positives is just about normal. So it seems to be well established throughout the drug using population of California.

Senator **Chiles**. To your knowledge is this strictly a California problem?

Mr. **Henderson**. We have two cases of overdose fatalities in Portland, OR, and one case in Arizona, but to my knowledge these are the only cases outside of California. I have looked at samples from other parts of the country but we have yet to see an overdose.

FENTANYL NOT EASY TO DETECT

Senator **Chiles**. Because of the similarity between the overdose death of an individual from fentanyl and one of these derivatives and heroin, it would be very easy for an autopsy to miss that or for people not to classify it as an overdose.

Mr. **Henderson**. Yes. They could classify it just as an unexplained death or as an unexplained multiple drug death. Any coroner cannot detect fentanyl. It will not be detected by classical chemical analysis.

Senator **Chiles**. The regular coroner examination will not detect this as a regular fentanyl death.

Mr. **Henderson**. No. It will look like a regular heroin or overdose case, but it is so unique—totally unrelated to any of the morphine based compounds like codeine or heroin.

Senator **Chiles**. What efforts have you taken to define the scope of the problem and what types of funding have you received to conduct this work?

Mr. **Henderson**. It has been difficult. We first knew that fentanyl was a drug being abused probably 10 years ago. It is a drug used for race horses. There is an interesting effect that narcotics stimulates animals like horses and cats and for years and years people have used narcotics to stimulate racehorses and fentanyl has been abused probably 10 years in the racehorse industry. We knew that that was occurring, but no one was terribly interested until recently when we found that it was being abused by humans.

I have had some funding from the State of California to allow me to analyze biologic samples from overdose cases. This has been rather hit and miss. It has been very limited and we have not had a systematic program. At the present time I am funded by the State of California and we are looking at essentially three types of samples. We get cases sent to us by a coroner's laboratory from overdose cases in which fentanyl is suspected.

We are getting urine samples from drug treatment programs so we can monitor their clients' use of fentanyl, and we receive some powder samples from law enforcement agencies. Using these three sources, we are trying to piece together the use and distribution patterns of fentanyl in California.

SYNTHETIC DRUGS ARE DRUGS OF FUTURE

Senator **Chiles**. Can you give me some idea as to whether you think you are getting sufficient funds and whether sufficient assets are now being directed toward really finding out the scope of the problem and trying to get on top of it?

Mr. **Henderson**. I don't think so. But my perspective is that synthetic drugs are the drugs of the future. It does not make sense to import a drug halfway around the world when you can make it in your home or backyard for a few hundred dollars. I think it is difficult for people really to grasp the implication of this and as yet there has not been sufficient funding or even attention to the problem.

Senator **Chiles**. What type of sophistication is needed to make one of these drugs?

Mr. **Henderson**. Well, although people are astounded by the fact that these drugs are thousands of times as potent as heroin, they are very old drugs. It is not high technology. It is medium-level technology. These drugs are made by relatively easy synthetic procedures. If I can go up to this table——

Senator **Chiles**. Yes, please.

Mr. **Henderson**. This is representative of the type of equipment one would need. It would probably cost you a few hundred dollars of equipment to set up a fentanyl laboratory. The chemicals can be purchased through any chemical company. This is an Aldrich Chemical book that lists thousands of compounds. These are common industrial chemicals. Some people have said, let's restrict the sale of the starting chemicals. This is not possible because they are basic chemicals of industry.

Senator **Chiles**. I could go and purchase any of these chemicals by just going to a drug company or to a drugstore?

Mr. **Henderson**. Through a chemical company.

Senator **Chiles**. There wouldn't be anything illegal about what I would be buying?

Mr. **Henderson**. No. Because you can use these chemicals to make anything from shoe polish to photoemulsions. We do know that there are a few unique chemicals used in the synthesis of these drugs and they are watched carefully. This equipment may look sophisticated, but you really don't have to use something like this. You can make a similar apparatus from very common glassware.

Senator **Chiles**. I don't even have to buy this?

Mr. **Henderson**. There are underground chemical handbooks that will tell you how to assemble such equipment, how to take refrigerator motors and turn those into vacuum pumps. So the apparatus is easy to get hold of it. I think it takes $200 or $300 worth of chemicals, another few hundred dollars in apparatus and in 2 or 3 weeks time we could make a handful of material. One handful of 3-methyl fentanyl would be about 200 grams. I estimate that is about 200 million doses of fentanyl.

Senator Chiles. In 2 weeks you could make 200 million doses?

Mr. **Henderson**. Yes. The problem is——

Senator **Chiles**. For how much money?

Mr. **Henderson**. $1,000, $2,000 tops.

Senator **Chiles**. $2,000 tops, you could make 200 million doses?

SOPHISTICATED CHEMIST REQUIRED

Mr. **Henderson**. The key is not killing yourself in making it. It takes a very sophisticated chemist to do it right. The synthetic steps are easy, but dilluting it is high technology. The person who can dillute that out is a very sophisticated chemist. The quality control is remarkable. In a fentanyl series we find extremely pure, extremely sophisticated compounds that are made with amazing quality control. These are not being produced by you usual speed laboratories or PCP laboratories.

Senator CHILES. Where you fall short of that, you have impurities and the dangers. That doesn't mean someone is——

Mr. HENDERSON. Right now it is in the hands of very sophisticated people. But I am sure there are a lot of people looking on with interest who are much less skilled.

Senator CHILES. What are the kind of steps you would go through?

Mr. HENDERSON. You would order the chemicals and put them in a flask like this, heat them up. We call this step reflyxing. Then you take off the solvent. If you try to take the solvent off on top of a stove you get an explosion. The final step is of purification. Eventually you dry the material, in a watch glass like this, and that is it. We are purposely leaving out a very few critical steps. But any lab that can make PCP or the amphetamines can make the fentanyls.

Senator CHILES. You said that for $2,000 you could make 200 million doses. Would one dose be like a heroin dose?

Mr. HENDERSON. Yes.

Senator CHILES. What would that sell for?

Mr. HENDERSON. That is variable. You can see sell it as Persian white and say it is the purest heroin you ever had in your life. It was purchased from a person as he stepped off the plane from Tehran. That would sell for $300, $350. Or we might call it China White, and the color would be slightly off-white, perhaps a tanish color. We would say this is just very pure heroin and it might sell for $200. We could sell it as synthetic heroin, the stuff you have been reading about in the papers, at a bargain range of $15. Also, chemists can take the lactose, heat it up and turn it a brown color, mix it with fentanyl, and call the product Mexican brown.

Senator CHILES. So you could make this look like heroin so an addict wouldn't have any way of knowing?

Mr. HENDERSON. We could sell it for $300 or $30 a dose and it essentially costs pennies to make.

Senator CHILES. We are talking about something like millions and millions of dollars—200 million doses——

OVERDOSE CASES ARE OCCURRING IN SUBURBS

Mr. HENDERSON. The limiting step is then one of distribution. How do you distribute this much material. I think this is where we are getting very, very interesting findings.

The fentanyl overdose victims in California that we have studied are very typical of heroin addicts anywhere in the country except for one thing and that is the overdose cases are not occuring in our large cities. We have never had an overdose case in Los Angeles. Only two have occurred in San Francisco. The overdoses are occurring in the suburbs. The largest sample of China White I have analyzed was about the size of a loaf of bread and it was obtained in a rural community of about 1,300 people——

Senator CHILES. Was that real heroin?

Mr. HENDERSON. No. This was fentanyl. It was ready for sale, and it was found in a small town of about 1,300. It had been sent by parcel post from San Diego. These drugs can be distributed anywhere. All of our overdose cases are coming out of the suburbs, even rural communities. It is not a big city phenomenon.

Senator CHILES. What is the potential for organized crime to get involved in the designer drug market?

Mr. HENDERSON. That is the curious thing. In California it looks like at the present time it is a stand off. It looks as if organized crime has control of the big cities with their heroin and we have these new entrepreneurs operating in the suburbs.

Senator CHILES. Organized crime is using their existing flow and existing distribution center——

Mr. HENDERSON. Fentanyl distribution could be a parallel industry. In fact, many people speculate if the underground chemists are caught, they will be caught by the Mafia, rather than by law enforcement.

Senator CHILES. There is speculation that the Mafia is already trying to break into their industry?

Mr. HENDERSON. I don't know, but it does look like they are competing.

TREATMENT FACILITIES ARE FRUSTRATING

Senator CHILES. Are treatment facilities able to deal effectively with this problem?

Mr. HENDERSON. Not really. It is very confusing for the staff when they have people coming into treatment facilities that look like heroin addicts and act like heroin addicts, but they cannot find any traces of heroin in their blood or urine. They can't enroll them in addiction programs because they can't show proof of addiction. They know some of their people are abusing drugs but their urine analysis always comes back negative. It is extremely frustrating for treatment facilities. They simply have no handle on this problem.

Senator CHILES. What is the likelihood in your mind that this problem will get bigger?

Mr. HENDERSON. We know there are two or three more fentanyls that are waiting in the wings. We probably will have 10 fentanyl in California, probably by the end of this year. There are some very recent trends that are very alarming, the fentanyls are being mixed with other drugs. We find samples that are fentanyl cocaine mixtures, called speed balls. Also, fentanyl is being sold in two forms. One for shooters and one for snorters. They are becoming popular as drugs that are abused by snorting and inhalation as well as by injection. I think this has the potential of opening up an entirely new population of users, people who want to hide their addition, or who don't like needles.

Senator CHILES. Basically, a heroin addict has to use a needle as opposed to cocaine?

Mr. HENDERSON. Yes. A few people snort heroin and smoke heroin but basically it is injected. There seems to be a strong link between cocaine and fentanyl in some areas. Some people say they will not free base cocaine unless they have fentanyl to take the edge off. I think there may be a new type of addict emerging.

Senator CHILES. Who can presently test for fentanyl?

Mr. HENDERSON. Well, there are a few law enforcement laboratories that now test for fentanyl. But as for biological samples, I believe I am the only laboratory. With fentanyl we are talking about seven different chemicals that may only be present in parts per billion and parts per trillion. They are present in incredibly small amounts.

Senator CHILES. So the normal lab that hasn't been looking for this and doesn't know anything about this would not pick it up?

Mr. HENDERSON. Even in an overdose case a conventional lab would not detect fentanyl.

INSTRUMENT TO COORDINATE ACTIVITIES NEEDED

Senator CHILES. What would you consider to be an integrated approach or partnership between the education, the medical and law enforcement communities? How would you go about undertaking such an approach?

Mr. HENDERSON. Well, I think there should be a China White desk somewhere. There needs to be a person, a desk or a bureau or an instrument——

Senator CHILES. A China White desk?

Mr. HENDERSON. An instrument to coordinate the activities. I believe we have a lot of information available but essentially we just share stories over coffee. There is no coordinated effort between law enforcement people, medical people, and chemical toxicologists. We need a lot more information and we can get this by more systematic monitoring of drug overdose cases, and by monitoring confiscated powder samples, specifically for fentanyl. I think there should be a lot more cooperation between State agencies and agencies of the Federal Government. Until now it has been viewed as a California problem. California kookiness that we hope will go away. I don't think this is so and the problem will probably spread to the rest of the country.

AWARENESS IS FIRST STEP

Senator CHILES. How should the Federal Government comprehensively deal with the designer drug problem? Should we be providing the leadership and acting as the catalyst to try to put this effort together?

Mr. HENDERSON. I definitely think so. I think awareness is a first step. It seems we are still watching reruns of the French Connection while there is someone out there is using a computer to search the chemical literature of the world looking for new drugs to synthesize.

Senator CHILES. Essentially what you are saying is we think about smuggling of drugs through the ports and how someone is bringing it in and we are not worrying that someone with a computer is working out a formula with a new analog and it is going to be done in a highly sophisticated lab somewhere.

Again, I thank you very much for your testimony and I wonder if you would hold up that beaker again and show me what 200 million doses would be. I have done a little arithmetic. If that was Persian White, we would be talking about $70 billion worth of drugs that would be put in that dish?

Mr. **Henderson**. 200 grams is about like a handful of flour or a handful of salt. That is about 200 million doses.

Senator **Chiles**. That could be $70 billion?

Mr. **Henderson**. I could smuggle enough fentanyl soaked into the tab of my collar to supply this room for quite awhile. It could even be smuggled under a postage stamp.

Senator **Chiles**. We thank you very much for your testimony.

[The prepared statement of Mr. Henderson follows:]

THE PHARMACOLOGY AND TOXICOLOGY OF THE FENTANYLS (CHINA WHITE)

By

Gary L. Henderson, Ph.D.
Department of Pharmacology
School of Medicine
University of California
Davis, California 95616

SUMMARY

The fentanyls are a class of very potent narcotic-analgesics originally synthesized by the Janssen pharmaceutical company of Belgium. Although the chemical structures of these drugs are quite different from the opiates and opioids; the fentanyls, nevertheless, possess all the pharmacological and toxicological actions of the classical narcotics. Fentanyl, the parent drug, is used extensively in clinical medicine as an intravenous analgesic-anesthetic under the trade name Sublimaze and three derivatives are now in clinical trials in the United States and may be available in the near future as pharmaceuticals.

Beginning in 1979, illicitly synthesized derivatives of fentanyl began appearing on the streets as drugs of abuse under the name "CHINA WHITE", the name usually associated with very pure Southeast Asian heroin. Soon thereafter a series of deaths occurred in southern California which looked like typical heroin overdose deaths except that toxicological analysis failed to detect any narcotic. To date over 60 such deaths have occurred.

Our laboratory, using very sensitive analytical techniques specific for the fentanyls, has detected various fentanyl derivatives in the body fluids of the overdose victims. In addition, we have detected the fentanyls in the urine of a significant number of individuals enrolling in various methadone and other drug treatment programs throughout California.

To date we have identified five different fentanyl derivatives, in addition to fentanyl itself, in samples being sold illicitly under a variety of names such as "China White", "Synthetic Heroin" and "Fentanyl". The newest derivative, 3-methyl fentanyl, is extremely potent (approximately 3000 times as potent as morphine) and is thought to be responsible for an alarming number of recent overdose deaths in the San Francisco Bay area.

FENTANYL DERIVATIVES USED MEDICALLY (Figure 1)

A brief description of the fentanyl derivatives used in human and veterinary medicine is given below.

FENTANYL

Fentanyl was introduced into the United States in 1968 as an intravenous analgesic-anesthetic under the tradename Sublimaze® or Innovar® (the combination of fentanyl and droperidol).[1] Fentanyl now occupies a major place in therapeutics as a preanesthetic medication, an anesthetic, and a post-surgical analgesic. Fentanyl is very potent (approximately 100 times as potent as morphine) and short acting (duration of action is approximately 30 minutes). It is a very important drug clinically and is probably used in over 70% of all surgeries in the United States.[2]

THE ILLICIT ANALOGS (Figure 2)

Very little is known about the biological effects of the illicit derivatives. At best only preliminary data is available from studies conducted in laboratory animals. Virtually nothing is known about their effects in man.

ALPHA-METHYL FENTANYL

Alpha-methyl fentanyl was the first illicit fentanyl derivative to appear on the streets. It is a very simple modification of the fentanyl structure and is about 200 times as potent as morphine. As a new drug entity it was not at first on any international, federal or state restricted drug list and was in essence "street legal". However, it is now classified as a Schedule I drug (no approved medical use and high addiction liability) by the D.E.A.

PARA-FLOURO FENTANYL

Para-flouro fentanyl was the second illicit derivative to appear on the streets. It is a very simple derivative of fentanyl and has about the same potency. It is presently classified as a Schedule I drug by the D.E.A. Little is known about this compound. It appeared only briefly and does not seem to be in use at this time.

ALPHA-METHYL ACETYLFENTANYL

Alpha-methyl acetylfentanyl first appeared on the streets in 1983. This also is a very simple derivative of fentanyl, but because technically it is a new chemical entity, it escapes classification as a restricted drug. At this time (11/1/84) it is not a restricted drug. Nothing is known about its pharmacological properties.

ALPHA-METHYL FENTANYL ACRYLATE

Alpha-methyl fentanyl acrylate (this is a trivial, not a commonly accepted or generic name) has been identified in samples containing acetyl alpha-methyl fentanyl. It may be a new derivative but is more likely a contaminant or a by-product of synthetics. Nothing is known about its pharmacological properties.

BENZYL FENTANYL

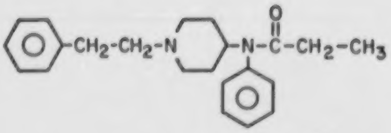
Benzyl fentanyl has recently appeared mixed with other fentanyl derivatives in street samples. It is possibly an unwanted synthetic by-product or an intermediate used in the synthesis of other fentanyl derivatives. It has no narcotic effects.

FENTANYL

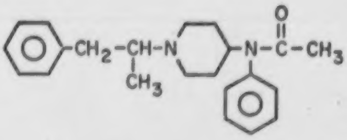
Fentanyl itself has appeared in street samples and has been associated with overdose deaths in California. It is most likely that the fentanyl sold on the streets is synthesized in illicit laboratories and not diverted from pharmaceutical supplies. All fentanyl sold on the streets is in powder form and all fentanyl sold as a pharmaceutical is in dilute, liquid form. Abuse of Sublimaze® in hospitals and clinics by medical personnel has been documented but the extent of the problem is not known.[3]

3-METHYL FENTANYL

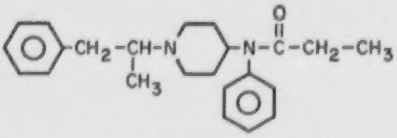
3-Methyl fentanyl is the latest derivative to be introduced onto the streets and it is certainly one of the most potent of the fentanyls (3000 times as potent as morphine). This analog appeared in California sometime between the Fall of 1983 and the Spring of 1984 and is thought to be responsible for over a dozen recent overdose deaths in the San francisco Bay area, the highest incidence of fentanyl-related deaths to date.



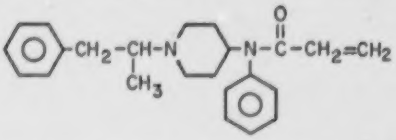
fentanyl (Sublimaze®)



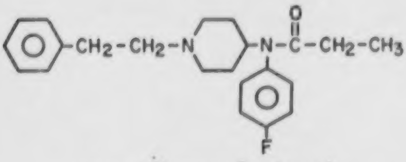
acetyl alpha-methyl fentanyl



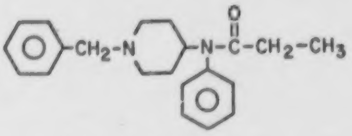
alpha methylfentanyl



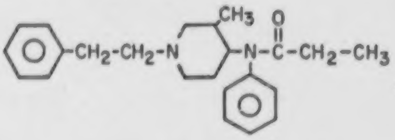
acryl alpha-methyl fentanyl



para-fluoro fentanyl



benzyl fentanyl



3-methyl fentanyl

FIGURE 2

SUFENTANYL

Sufentanyl is an extraordinarily potent derivative (2000-4000 times morphine) presently undergoing clinical trials as an anesthetic-analgesic agent for cardiac surgery.

ALFENTANYL

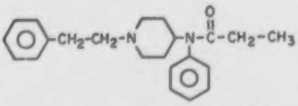
Alfentanyl is a very short acting (15 min.), slightly less potent derivative (20-30 times morphine) currently in clinical trials as an ultra-short acting analgesic to be used in diagnostic, dental, and minor surgical procedures.

LOFENTANYL

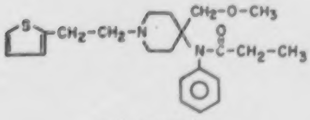
Lofentanyl is extremely potent (6000 times morphine) and very long acting and is being evaluated for use when prolonged analgesia and respiratory depression are required such as in tetanus and multiple trauma.

CARFENTANYL

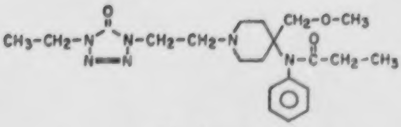
Carfentanyl is a very potent analog (3200 times morphine) which is used only in "capture guns" for immobilizing wild animals.



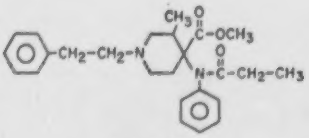
fentanyl (Sublimaze®)



sufentanyl



alfentanyl



lofentanyl

FIGURE 1

PHYSICAL DESCRIPTION OF "CHINA WHITE"

The fentanyls are cut (diluted) with large amounts of lactose or sucrose (powdered sugar) before they are sold on the street so the amount of active drug present is exceedingly small, less than 1%. These amounts are so small they contribute nothing to the color, odor or taste of the sample.

COLOR

The color of the samples obtained to date has ranged from pure white (sold as "Persian White") to light tan (sold as "China White", "Synthetic Heroin", or "Fentanyl") to light brown (sold as "Mexican Brown"). The brown color comes from the lactose which has been heated and has carmelized slightly.

TEXTURE

The texture of the samples observed in our laboratory has ranged from light and finely powdered to somewhat coarse, cakelike and crumbly, somewhat resembling powdered milk.

ODOR

Occasional samples will have a medicinal or chemical odor, but this is not characteristic.

In summary, the fentanyls appear in all the various forms that heroin does and there is nothing characteristic about the appearance of any sample that will identify it as fentanyl.

ROUTES OF ADMINISTRATION

Intravenous injection is the most common route of administration for the fentanyls; however they also may be smoked or snorted. In fact because of their high lipid solubility, the fentanyls should be excellent drugs for snorting and may become increasingly popular drugs among cocaine users. At least one overdose fatality was identified in which snorting was the only route of administration. We have also been able to detect fentanyl in the urine of individuals who used the drug only by smoking it.

PHARMACOLOGICAL EFFECTS

It should be remembered that although the fentanyls are chemically quite distinct from other narcotics (morphine, heroin, methadone etc.), they are pharmacologically equivalent; that is they have all the effects, side effects and toxic effects of the clasical narcotics. Therefore all the actions of the fentanyls can be reversed by naloxone (Narcan®), although higher doses of the antagonist may be required.

EUPHORIA

The euphoria or "rush" from the fentanyls should be qualitatively similar to that of heroin and the intensity of the effect would depend upon the dose and the particular derivative used.

ANALGESIA

Profound analgesia (absence of pain) is a characteristic effect of all the fentanyls. As little as 50 micrograms of fentanyl will produce analgesia while only 3 micrograms of the 3-methyl derivative would be required.

SIDE EFFECTS AND TOXICITY

RESPIRATORY DEPRESSION

Respiratory depression is the most significant acute toxic effect of the fentanyls. The depth and duration of respiratory depression will depend on the dose and the derivative used. However, compared with other narcotics this effect is relatively short-lived. For example, following 200 micrograms of fentanyl given intravenously maximum depression occurs within 5-10 minutes, and normal respiration returns within 15-30 minutes.

ANTIDOTE

Naloxone (Narcan®) is the antidote of choice for respiratory depression (or any other effect) produced by the fentanyls

BRADYCARDIA

Fentanyl produces a dose-dependent decrease in heart rate of up to 25% with a parallel drop in blood pressure of up to 20%. This effect is thought to be due to vagal stimulation and can be blocked by atropine. The role of this response, if any, in overdose deaths is not known.

MUSCLE RIGIDITY

Muscle rigidity, particularly in the chest wall, sometimes called "wooden chest" is a response common to high doses of all narcotics. Individuals using the fentanyls may describe this effect as a muscle tightness or tingling.

ADDICTION LIABILITY

The fentanyls produce both tolerance and physiological dependence following repeated administration. Controlled studies have shown that addicts perceive fentanyl subjectively as having heroin-like effects. In California we have found many individuals enrolling in methadone treatment programs who have only fentanyl in their urine upon admission, yet are convinced they use only very high grade heroin. Therefore when pharmacologically equivalent doses are used, most users probably cannot tell the difference between heroin and the fentanyls.

ABUSE POTENTIAL

Fentanyl as a pharmaceutical (Sublimaze®) was always thought to have a low abuse potential because of its short duration of action and its restricted availability. Also, Sublimaze® is available only in injectable, aqueous formulations containing either 100 micrograms or 500 micrograms per vial (50 micrograms/milliter). These relatively small amounts and low concentrations make it difficult for a tolerant addict to administer a euphoric dose conveniently.

Until now, the only documented illicit use of fentanyl was in "doping" race horses. Narcotics are frequently used to dope horses because they produce excitation in the horse (and other animals such as the cat and mouse). Fentanyl's short duration of action and its very low, difficult to detect, concentrations in blood and urine make it an ideal doping agent. Fentanyl has been used in this manner for nearly a decade.

Now the fentanyls are available throughout most of California and because they are potent, not detected by routine analytical methods, and, in the case of the newer analogs, quite legal, they may become the drug of choice for many heroin users. It is the opinion of this author that fentanyl use will increase in California, its use will spread to other states, and that new derivatives will appear periodically.

OVERDOSE DEATHS

To date my laboratory has identified over 50 overdose deaths caused by the fentanyls. Nearly all of these cases occurred in California; however, two recent deaths occurred in Oregon which suggests that fentanyl use may be spreading to other states. All cases were similar in that they involved known heroin users, injection sites and accompanying paraphernalia were found, and autopsy showed typical signs of narcotic overdose such as pulmonary edema and congestion. Routine toxicological analysis of the body fluids revealed no narcotics, sedatives or stimulant drugs present; however, analysis of these fluids in my laboratory using methods specific for the fentanyls revealed very low levels (1-10 nanograms/milliliter) of these drugs. Traces of the fentanyls were also found in the accompanying paraphernalia.

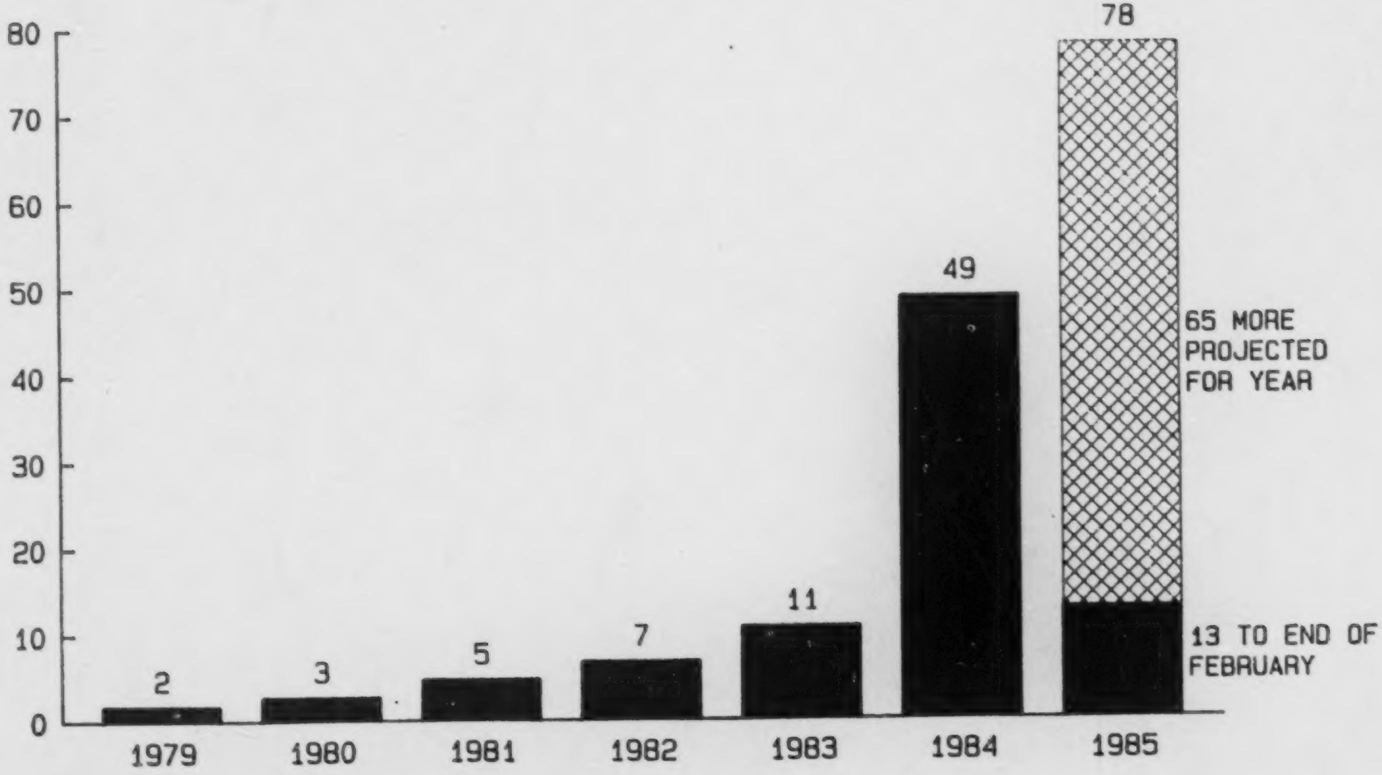
Fentanyl-related deaths have occurred in nearly every urban area in California, in suburban areas, and even in semi-rural areas. Ages of the victims ranged from 20-49 years. Most were male, although 9 were female. Most of the victims were white; but there were significant numbers of hispanics and blacks. In short, fentanyl use is not confined to any geographic area or any social, economic or ethnic group, but is distributed widely throughout the heroin using population.

PHARMACOKINETICS

Fentanyl is very lipophilic and distributes from blood to body tissues very quickly. In fact, 10 minutes after IV administration, 98% of the dose will have disappeared from the blood. Maximum brain concentrations are reached equally as fast, usually within 1 minute. This explains the very fast onset of action. The short duration of action is explained by the ease in which the drug is washed out of the brain and distributed to other tissues.

The disappearance of fentanyl from the blood is best described as a three step process: first, fentanyl distributes rapidly to other tissues ($t_{\frac{1}{2}}$= minute); secondly, fentanyl is metabolized by the liver and excreted in urine and feces ($t_{\frac{1}{2}}$=10 minutes); and thirdly, as blood levels of the drug fall, the drug redistributes from tissues back into blood where it is metabolized and excreted ($t_{\frac{1}{2}}$=2-4 hours).[4,5]

NUMBER OF FENTANYL DEATHS



Senator **Chiles**. Our next witnesses will be Mr. and Mrs. Donald Kidston.

Mr. and Mrs. Kidston, we appreciate you being with us this morning. I know the story you have to share is not an easy one. I know you are from Bethesda, MD, since Mr. Kidston retired from the State Department's Foreign Service.

The second of Mr. and Mrs. Kidston's children died in 1978 from an overdose of cocaine. He died on the National Institute of Health's campus in Bethesda. I think his story is very important to us and what we are talking about here—the dangers in designer drugs.

We appreciate very much your being here. Mrs. Kidston, if you would tell us that story.

STATEMENT OF GERALDINE AND DONALD KIDSTON, BETHESDA, MD

Mrs. **Kidston**. Thank you. It is a difficult story to tell, but thank you for this opportunity. I hope this will help someone else along the line.

Barry was about 3 months old when we took him overseas. We had 20 years of assignments out of this country. In interesting countries. We liked them very much. We went to the Philippines first.

INTRODUCED TO DEMEROL AT 14

I won't mention all of the countries because I don't think it is important, but when Barry was about 14 years old he had a serious automobile accident and fractured both wrists and his left tibia. While there he was treated with Demerol for pain relief.

In 1966 I don't believe we knew too much about Demerol and how addicting it was. We went back to Manila when my husband was assigned to Saigon. We went back as a safe haven from Turkey. My husband's assignment was in Saigon.

We came back to the States in 1968. Both of our children at that time had really not spent any time at home other than a few months of home leave. Our son went to Western Junior High School in Bethesda and at that point the principal called me and said I should come up. They said they had taken some medicine from Barry. Some diet pills that I had at the house. I had no idea that those diet pills contained what they did. We gave Barry psychiatric help. We sent him off to a prep school hoping that things would work out and that he would get his feet on the ground. He wasn't at the prep school very long when he was into drugs and he came home.

We stayed in the States until the early part of 1971 when we were reassigned to New Delhi, India. Drugs were very easy to obtain and Barry, unfortunately, got into the scene out there. He did graduate from the American School in New Delhi. He was accepted at Boston University, at George Washington University, at High Point College in North Carolina.

Unfortunately, the situation with the drugs in New Delhi became so bad that my husband and the family were asked by the State Department to come back to the United States, which we did.

We came back in May of 1972. My husband retired in June 1972. When we came home, because of the drug situation, we had discussions with the doctors at the State Department, the medical division of the State Department and they told us that they felt that they would kick Barry out of the house and let him go his own way because he brought this on himself. We felt, however, that we should give Barry all the help we could through psychiatric care and our own family love. We felt at that point things were in a closet. You didn't talk to people about it. You didn't tell them this is what was happening to your son or what was happening to you and your family.

Barry seemed to get along fine. In the fall of 1972, he decided to go to High Point College in North Carolina. He seemed to straighten out and got serious about school. He was there until 1975, in December, but he had an incident, breaking and entering and stealing drugs from a drug store. Well, High Point College asked us to bring him home, which we did.

STARTED LABORATORY IN BASEMENT

In January 1976 Barry was enrolled at GW with a major in chemistry. He was an intelligent young man. He had a great personality. Of course, I am a little biased on that because he was my son but I still thought a great deal of him. He got along well with people. He liked to help people and do things. He was outgoing, but he then started a laboratory in our basement.

Our basement is not very large. It is a room where I have a sewing machine and a washer and dryer and the usual gas furnace and that sort of thing. He decided to make some—do some experiments. Basically he told us they were for class, to help him in his class work at GW, and also to try to develop a synthetic Demerol, which would be a nonaddicting Demerol. I don't think at that point we realized how serious he was into the drug field or not. I don't know. But as we know now, what he did do, I guess he got into what we are now calling designer drugs.

He didn't even have as fancy a gadget as that thing up there. He had a little Aetna burner. He had flasks and beekers, and he had one of those glass trays that I see. In fact, I have a little note about that being washed in my dish washer, not realizing what was being washed. He bought chemicals from mail order houses. He ordered chemicals from chemical supply houses in the Rockville area. He bought—I bought chemical books for him, rather expensive ones but he felt he needed them for George Washington school and he also went to various libraries and researched what he needed. He went to NIH Medical Library and the other one across from Bethesda Naval Hospital and he would Xerox formulas and descriptions and pictures and bring them home and work on them.

He worked really on top of my washing machine and when I would go to wash, I would give him the devil because he hadn't cleaned up so I could get at the top of my washing machine. He also used the dishwasher for washing various chemicals. He would bend back the prongs that hold up the glasses.

We didn't realize what he was doing until the 30th of September in 1976 when a boil erupted on his arm. I took him over to Bethesda Naval Hospital and he told the story, and he told me the same story, that bees had stung him a couple of weeks prior to that and the stingers were still in his arm. Bethesda treated him, sent him home and that healed. But in November 1976—he wasn't going to school at that point, he had dropped out of George Washington—he showed some signs of being lackadaisical around the house or not being enthusiastic about anything and then one day he couldn't bring his arms down out of the air.

Senator **Chiles**. Couldn't bring his arms down out of the air?

Mrs. **Kidston**. He was stiff. He was walking with a very peculiar gait. I took him to a psychiatrist who I knew and who had been working with us, and who knew the family situation, background, the whole story. He didn't know at that point about the chemicals that Barry had been making. Barry was put in Sibley Hospital. He was there approximately 4 weeks. He was completely catatonic. He was diagnosed as a catatonic schizophrenic.

Senator **Chiles**. Catatonic schizophrenia was the diagnosis?

Mrs. **Kidston**. Yes. They did give him electrical shock treatments with our permission, and then there was a discussion that they felt it was not a catatonic condition, that it could be a neurological problem. At that point we started getting into the Parkinsonian syndrome which is what they said it could be. Navy talked to him but referred him to NIH and at NIH they gave him some treatment as an inpatient and outpatient, both the psychiatric department, the neurological department, everybody was involved in it. When he was on out-patient he would be home with us.

DIFFICULT TO LIVE WITH

It was difficult living with him. He would not sleep well at night. He seemed to sleep well during the day but not at night. I would sit up and play chess with him—not chess, I can't remember what it was—until 3 or 4 in the morning, but I had to go to bed because I had to get up and go to work the next morning.

That continued until in November—the summer of 1978, when I was working in the garden. My husband came out and told me he had to call the police, that Barry had threatened him. The police came. We had quite a to-do about it because Barry had a gun in the house. The police came in and talked to us after they settled him down. We worked everything out, but we told Barry he had to leave.

He moved over to Greenbelt with a friend who unfortunately was heavy into cocaine but Barry at that point—well it was a matter of living with the cocaine or he would have gone out and gotten the cocaine. We really couldn't do much with him. He got a job in the Door Store in Georgetown. Living in Greenbelt he would miss the last bus, and he would call me and ask me, would I come and pick him up and take him home. I would do that.

Then on the 3d of September, that was a Labor Day weekend, he called. It was about 4 in the morning. He was over at the campus, University of Maryland campus, and would I come and get him. So I did. I picked him up and told him I would like to take him home. He said, let's pick up my laundry first. We went to his apartment. He went in to get the laundry. I waited for about 2 hours. I didn't know his apartment number, unfortunately. I waited until I saw a woman watering her flowers and went up and introduced myself. I called my husband and asked him for Barry's phone number. I called Barry and asked him his apartment number and I went upstairs and when I got up to the apartment, Barry was sitting on a commode and just slumped over. I thought he was unconscious. He wasn't. He was in a sort of stupor.

We got in the car and I took his laundry and we started out the beltway to Bethesda. I was furious with him and I let him know it in no uncertain terms but it didn't help much. I got a little of the steam out of me, I guess, and that morning we got back to the house. It was about 7:30. Barry went down to the basement. I wanted to get him breakfast. He wasn't interested, and he finally said he was going home. He called a friend that he lived with and the friend came and Barry and he left and the last I saw of Barry is as he walked out the door through the car port, smiling and waving goodbye.

About 6:30 or 7 p.m., we had a call from Bethesda Naval Hospital. They asked if Barry was our son. I said, yes. They said they are checking records. About 9 o'clock or 10 o'clock NIH called saying they wanted to know if Barry was our son. They said they were retiring records.

About 10 o'clock that night the front door bell rang and there were three gentlemen. One was from the coroner's office and one was from the FBI, and the other was a State trooper. The FBI was involved because Barry had been found under a tree dead on the NIH grounds.

DIED FROM OVERDOSE

Later, when we pieced some of the story together, we learned Barry had gone to a pharmacy across the street from NIH to buy some Robutussin cough medicine with codeine. Whether he ever got it or not, I don't know, except that the death certificate does show an overdose of cocaine and codeine. Maybe he did get the bottle. I think they come in about 8 ounces.

But at the same time, on a manila envelope he had written out his will of what he wanted done with what he thought was his share of what our estate would be when we were gone. I have all of that.

My husband didn't believe the people when they came to the front door and we asked them if they were sure. They had Barry's ring. It was a puzzle ring from Turkey. They had his wristwatch and they had a chain that he had worn around his neck and a few dollar bills and they had his car keys which I could identify because of a particular type of key ring he had.

They didn't have to ask us to identify the body. They had brought a Navy doctor in and they brought somebody in from NIH and they had identified the body, plus the fact that he had a vial of medication on his body which had his name on it with a prescription number from Bethesda.

They took him to Baltimore for an autopsy. And I called NIH and asked them if they would like his brain. I felt it would serve some purpose. With Parkinson's, I believed this would show up in the brain.

Senator CHILES. The Parkinsonian symptoms, they came from what he was doing in the lab, from the effect of the designer drugs?

Mrs. KIDSTON. He had made some batches of this and then we have learned since that one of the batches he was anxious for—it wasn't quite ready. It was improper, and when he injected himself with the medicine—now he never, to our knowledge, sold any of his medicine. He used it for his own purpose. This was a period of when he started, in 1976——

Senator CHILES. At the time you thought he was doing experiments that were good and you were encouraging him, and his professors were encouraging him. You were helping him buy the material; you didn't know he was trying to make drugs for himself?

Mrs. KIDSTON. We thought he was trying to make a nonaddicting demerol which was admirable.

Senator CHILES. And you saw the first signs of a boil which he said were bee stings?

Mrs. KIDSTON. I trusted him.

Senator CHILES. Was NIH ever able to determine—that he had Parkinson's symptoms which came from taking the drugs?

Mrs. KIDSTON. They never went from the point that it came from the drugs he made himself. They said it was from a heavy drug addiction.

Senator CHILES. They didn't know what he was doing?

Mrs. KIDSTON. No. But when the Navy referred him over to NIH, they referred it as Parkinson's syndrome.

Senator CHILES. But you found out earlier he had tried to make a batch?

Mrs. KIDSTON. Yes. That came out in an article that a young man wrote and researched in the Washington Times.

Senator CHILES. I understand you learned most about your son's problems and what he had been doing after his death?

Mrs. KIDSTON. That is correct. We knew he was on drugs and he needed help but we didn't realize the extent of what he had done or what he was doing.

NO DIFFICULTY PURCHASING MATERIALS

Senator CHILES. The material he was able to assemble for the little lab that he put in your laundry room, he was able to buy or he could send you to the store to buy. There was no difficulty in purchasing the glassware or the chemicals. Where did he get the chemicals?

Mrs. KIDSTON. From chemical supply houses located in the area. He would write away for them. I still have copies of those invoices.

Senator CHILES. The glassware, where did he get that?

Mrs. KIDSTON. From chemical supply houses and some of them would come in through the U.S. parcel service.

Senator CHILES. When did he experiment, when did he use this lab?

Mrs. KIDSTON. He started in 1976 and the symptoms started with the Parkinsonian in 1978, October 1978.

Senator CHILES. 1978 is when he had the symptoms——

Mrs. **Kidston**. Yes, the eruptions and the other——

Senator **Chiles**. Would he do this in the afternoon or what time?

Mrs. **Kidston**. I am not sure, because I was working at the time, which is a poor excuse. But I didn't know what he was doing.

Senator **Chiles**. You think he was doing this basically for his own use?

Mrs. **Kidston**. Yes, for his own use and to see if he could find a synthetic demerol.

Senator **Chiles**. Barry was a bright young man when he didn't have drug problems?

Mrs. **Kidston**. He was a bright, intelligent young man who destroyed himself.

Senator **Chiles**. You brought some pictures.

Mrs. **Kidston**. This is a picture of the family in 1973. My daughter, who was terribly hurt by the whole situation, was torn between her love for him and her disgust for anybody who would lower himself for the drugs. This picture was taken over by the Potomac in 1973 and this picture was taken when he was out in a village in India. That was taken between 1971 and 1972.

Senator **Chiles**. Actually, the first problem that he had with drugs is when he had taken some of your diet pills and that is when he was still—how old was he at that time?

Mrs. **Kidston**. Fifteen.

Senator **Chiles**. The Demerol dependency started after the accident?

Mrs. **Kidston**. That has been my thinking. I don't want to accuse somebody. There is a difference of opinion in the family about that.

SERIOUSNESS OF PROBLEM SHOULD BE MADE KNOWN

Senator **Chiles**. You have heard some of the testimony on the designer drugs and I think you now understand that your son was one of the earlier experimenters of designer drugs. What do you think the role of the Federal Government should be as we try to get on top of this problem?

Mrs. **Kidston**. I realize now after hearing the discussion here that it is more serious than I had ever realized. I thought Barry was an isolated case, but I think we ought to get on top of it and I think we should not put it into the closet. It should be out in the open and people should be made to realize the seriousness of this with small children. We have a grandson who is now 1 year old. We are taking care of him, and I look at him and shutter to think of what could happen in this country, for him to have to contend with, and I shutter for what is going to happen to our country if this takes hold of our American people, our young people. They will be just a bunch of walking zombies.

Senator **Chiles**. I think you are right when you say the time when you all were going through this problem there was no one to share it with. All of us try to hide that sort of thing, and I think we are now recognizing the extent of the problem and we need to get it out in the open. Of course, parents should understand the potential hazards we are talking about, and individuals must be alerted to the dangers of these drugs. It must have been horrible seeing your son in that kind of catatonic state.

Mrs. Kidston. It was. We have to start with the young people earlier, not 15 or 16. The education should begin in the home and should start right away. Just like we do with the poisons, not keeping them around, keeping them out of the kitchen cabinets, making sure they don't get into the ammonia.

Senator Chiles. We thank you very, very much for coming here and sharing your story with us. We certainly think it will help.

Mrs. Kidston. Thank you.

Our next witness is Dr. J. William Langston, chairman of the Neurology Department of Santa Clara Valley Medical Center.

Dr. Langston has been treating patients with Parkinson like symptoms obtained from designer drugs.

Dr. Langston, we again thank you very much for your attendance here. We know you have become a recognized expert in this field and we appreciate anything you can share with us in this regard.

STATEMENT OF DR. J. WILLIAM LANGSTON, CHAIRMAN, NEUROLOGY DEPARTMENT, SANTA CLARA VALLEY MEDICAL CENTER, SAN JOSE, CA

Dr. Langston. I would like to start by saying I was very moved by hearing Mrs. Kidston's comments. Barry's case was the first tragedy due to abuse of uncontrolled synthetic narcotics, but not the last.

I would like to say to them, that they may or may not want to see the tapes because I think it will be like seeing the nightmare again.

I am very gratified that this committee is looking into this problem. There are a number of us who have been saying the time to act is before this problem spreads. So often the Government, medicine, or other groups involved in the public interest do not act until the disaster has already occurred. We are living right now in San Jose, CA, in the center of such a disaster. We are calling it the first designer drug disaster and I would like to share with you what this has meant for the lives of a number of young people.

DESIGNER DRUGS HAVE MEDICAL HAZARDS

I am a physician, a neurologist. I would like to point out that while there is a great concern about the spread of these drugs and the fact that they may take over the drug market, there is another major problem to be worried about, and that is medical. There are three medical hazards to this new approach which has been called the designer drug phenomenon.

When illicit chemists make these new drugs, they do not have to go through the stringencies required of a legitimate pharmaceutical company. When they make a new drug, a pharmaceutical company must test it in animals years before it will be tried in humans. With these new synthetic narcotics, the first animals are street users. In other words, drug addicts become, in a way, human guinea pigs.

The second problem——

Senator Chiles. The animals are the poor addicts out there on the street thinking they are buying Persian White or China White and that is their monkeys, that is their guinea pigs, that is their rats that they are experimenting with and these things, thousands of times stronger——

Dr. **Langston**. Or poison. A drug company finds that out when they give it to rats. These people find out when they give it to humans, when they sell it on the streets.

Senator **Chiles**. The result is the deaths we are seeing.

Dr. **Langston**. And permanent crippling of many people. The syndrome has been called the living death and in some ways it is worse. At least some of the addicts have told us that.

The second problem is that of quality control. A drug company has to be sure that any product they sell is pure. Very few of these chemists have quality control. If they make a bad batch, again, the first people to find out are the addicts on the streets.

Senator **Chiles**. The bad batch is not thrown out?

Dr. **Langston**. No. It is sold again and again.

Senator **Chiles**. No waste product in this type of action.

Dr. **Langston**. An addict will not throw a high away.

The third problem——

Senator **Chiles**. An addict can't go complain either.

Dr. **Langston**. That is right. They will not complain.

The third problem is potency. Some of these drugs are terribly potent and it is very easy to overdose.

BYPRODUCT IS DEADLY POISON

What I will address is the Demerol line. You have heard about the fentanyl line. These are what we call Demerol-look-alikes. What we think happened is a chemist in the bay area researched the Stanford Library until he found the very same report that I think Barry Kidston used to make a Demerol-look-alike which is called MPPP, which was uncontrolled and could be sold on the streets without any fear of prosecution. We now know there is a byproduct in the synthesis of MPPP which is a deadly poison, and kills cells in the brain. In fact, it kills exactly the same cells that die in Parkinson's disease.

We began seeing young addicts that had literally frozen overnight. They looked like 70 or 80 years old with Parkinson's disease. Of course, as a physician, this was a remarkable thing to see. It set off quite a medical chase using law enforcement agencies, and any clue we could get our hands on. Eventually we were able to identify the toxic by-product in this heroin and that helped identify what it was Barry had taken.

Senator **Chiles**. Is there any doubt in your mind after listening to the testimony as to what Barry had done to himself?

Dr. **Langston**. No doubt. I am afraid, if the Kidston's are still here, they are going to have a real deja vu. When I found out about that paper, I had read two sentences and I knew it was the same thing, had to be the same thing happening again.

Senator **Chiles**. Exactly, you knew?

Dr. **Langston**. Yes. It took us 2 days to prove it, but what happened to Barry is identical to what I am going to show you.

What I am going to show you are some video tapes of these patients to give you an idea of the effects of MPTP. MPTP is the byproduct which contaminates MPPP, the Demerol-look-alike. It is the quality control problem when making MPPP that leads to this tragedy.

The first case I am going to show you is of a young woman who was, I believe, 26 at the time she used this. It was the summer of 1982 and this was the first time she had experimented with IV drugs. She had used drugs before but never IV. Over 6 days she lost interest, froze up and was taken to an emergency room where she was put on the psychiatric unit and diagnosed as having hysterical paralysis. She was in that psychiatric unit for 3 weeks and then sent home, and told it was all in her head. It was only when we identified the street heroin that a public health nurse watching the TV news recognized the symptoms and called us.

Senator CHILES. She was told this was all in her head?

Dr. LANGSTON. Right. It was thought to be just hysterical.

PRISONER IN OWN BODY

This young woman had been frozen, unable to move at all for 6 weeks when we saw her. She could not even make a sound. If you put your ear on her chest you could hear a faint sound. She had been a prisoner in her own body for 6 weeks. She was totally normal mentally.

This is another case. This gentlemen had used three doses of this compound.

Senator CHILES. If we can, I want to ask you about the woman. She was like that for 6 weeks?

Dr. LANGSTON. She was in that condition for 6 weeks. She had been in the hospital for 6 weeks. They thought it was hysterical because she became paralyzed when her boyfriend became paralyzed. It didn't take us long to realize that the boyfriend had used MPTP too.

Senator CHILES. They said they were both——

Dr. LANGSTON. They were both using heroin. Again, to point out the horror she must have felt for 6 weeks not being able to say a thing. There is no facial expression.

Senator CHILES. How do you know?

Dr. LANGSTON. Once we treated her, she could talk. She remembered everything.

Here she is trying to stand. She is trying as hard as she can to stand up.

This patient was somewhat less affected but you will see this is a classic Parkinsonian posture, someone walking with a slow, shuffling gait. This is two mornings after he ran out of the substance. He woke up frozen and couldn't remove his arm from his girlfriend. He is trying as hard as he can. All you can see is a little shaking. This man was totally normal mentally. He can get up if he has assistance. It is not really paralysis. It is the inability to initiate movement.

Here you see the blank facial stare, and drooling. And here he is being asked to stick his tongue out. He is trying and you will see it takes him 30 seconds to protrude his tongue.

You see the fixed stare.

The next young man has a severe tremor which still persists. He could not lift a fork to his mouth.

CONDITION IS PERMANENT

Senator **Chiles**. You said was and still is?

Dr. **Langston**. This is a permanent condition. I will get into that in 1 minute.

Shall we continue?

This is about as severe a tremor as you are likely to see in Parkinson's disease. This next young man is absolutely frozen halfway out of getting out of bed. He used this for about 2 weeks, he and his brother, until the point they could no longer move and they probably would have starved to death had it not been for their mother who stopped by to see them. You can see, again, the complete loss of facial expression. The voice is diminished. This was a very athletic young man before using this substance.

We started these patients out on L-Dopa out of desperation. That is the same drug used for Parkinson's disease. This young woman is the same one we saw before. She has her facial expression back. She can smile. The medication, L-Dopa probably saved her life. She would have died without it.

These patients did respond to the same medicine we use in Parkinson's disease. However, the condition is permanent and anyone who knows Parkinson's knows that with time that the efficiency of the treatment wears off and you get to a point where either the medicine wears off rapidly or you get intolerable side effects. At that point we say the therapeutic window is closed.

When someone is 80 or 90 years old and we reach that stage, that is tragic enough. But for these young people, they have all developed these side effects within weeks and months and several now, we have reached really a desperate stage where there is no time that they are really normal. I will show you two examples.

Senator **Chiles**. Even those that you were able to help, that help is only for a period of time, and then it starts wearing off and you don't have anything else to treat them?

Dr. **Langston**. Yes; when you start somebody on therapy when they are 65 and you get these problems when they are 75, you can make your peace with that. But when you start it with somebody who is 25 and they are this way when they are 26, it is very difficult.

Senator **Chiles**. The drug and the treatment is good for about 1 year?

Dr. **Langston**. Yes; it is worse than that. Because they start out with such severe symptoms. This is one of the most dreaded effects. You get too much movement instead of too little and it could be quite disfiguring.

This is just 5 minutes later. You can see the twisting, writhing movements. She has now lost 50 pounds, because of these movements, which are uncontrollable.

Senator **Chiles**. That is a side effect?

Dr. **Langston**. A side effect of the medication. Usually we don't see it within 5 years. She got it within 3 weeks. You have to drop the medicine down. Then the patient freezes up and you can't move and you are between a rock and a hard place therapeutically speaking.

MEDICATION WEARS OFF

The other big problem with L-Dopa is a wearing off effect. The medicine works shorter and shorter periods. This is 2 p.m., the patient has received his medications. It is now 4:22 p.m., 2½ hours later. As a neurologist if he walked by me on the street I wouldn't notice anything particular about him. This is less than 20 minutes later and you will notice, it is like seeing Parkinson's evolve in front of your eyes.

Senator **Chiles**. This guy was an athlete and he is trying to exercise?

Dr. **Langston**. Yes; notice this is just 18 minutes later and he is already slowing down. The medicine is already wearing off. He has only gotten about 2 hours of relief. The time is 9 minutes later, 4:49 p.m.

You can see, he is completely unable to move—the only thing he can move are his eyes. This man now has to take medicine every 1 hour and 45 minutes to be able to function at all.

We are not optimistic about the future of a number of these patients because of the problems we are having. The human body can't last very long in this condition. We now are aware of over 400 young people who used these drugs in northern California. Most of them are currently asymptommatic. They used it several times and have stopped. Seven are in this condition. Another 20 have mild Parkinson's. However, there are scientific reasons to fear that all of these young people may be at risk for developing a Parkinson's like condition in the future. In fact, they have been referred to by a senior investigator at NIH as walking time bombs.

If in fact some of these people come down with Parkinsonian syndrome in the future, the social and human suffering and financial costs will be tremendous.

Senator **Chiles**. Can you tell me what the cost of these seven patients is?

Dr. **Langston**. If they require nursing home care, the average yearly cost is $20,000. Multiply that by 400. If they have to go to acute care hospitals, the number is higher than that.

EFFECTS ARE UNKNOWN

Given the approach that I started out describing, when you make a new compound, you don't know what its effects are. This is the first designer drug disaster, and unless something is done, I fear there will be more.

Senator **Chiles**. You mean that it could be worse?

Dr. **Langston**. It could damage other areas of the brain or organs. I don't know how it could be worse. If you are going to have to live, it is hard to pick a condition that could be much worse. Unless something is done, the more we will see disasters. Everybody knows, a lot of young people experiment. We hope that most young people get through that stage of their life intact, but with these potential poisons, anyone who takes a street drug is playing Russian roulette with their brain.

Senator CHILES. Does the abuse of MPPP offer a serious threat to law enforcement and the general public?

Dr. LANGSTON. It could. We know of some chemists who are using this who developed Parkinson's. You can inhale it. I would be very nervous using it. It can evaporate at room temperature. If you are in a room and leave the lid of the jar open, it evaporates.

I may say as an aside, one the fascinating parts of this is it is conceivable this may help us to understand Parkinson's disease and it is even conceivable that a compound like this is in the environment and is a cause of Parkinson's. So there are other major medical ramifications.

Senator CHILES. You are saying that Parkinson's disease itself may have been caused by some compound, chemical thing in the atmosphere?

Dr. LANGSTON. That is conceivable. There is a great deal of excitement in the medical community right now.

One point I would like to make is that originally we had found about 70 exposed cases. We have gotten help from CDC, the Center for Disease Control. That is why we know of about 400. When they left in January, I think they left in almost a state of retreat. They were finding so many new cases, that we are overwhelmed. I think we are touching the tip of the iceberg in northern California.

Senator CHILES. They are no longer seeking to help you, seeking to find out if there are additional cases.

Dr. LANGSTON. We are desparately seeking that. We hope CDC will continue to help us. We are living with this every day. I see this. It is a heavy burden. How are we going to handle this? How are we going to track down the other people at risk and give them care? We are doing it on our own, nights, weekends. But I feel this is a situation that should be studied because it is the first major health problem to come out of this designer drug era. It is a chance to learn how to deal with this and how are we going to handle or deal with the next one.

MPPP STILL BEING SOLD ON STREET

Senator CHILES. Do you believe that MPPP is still being sold on the street or is it a one time accident?

Dr. LANGSTON. We know for a fact after about a year's quiet, it was made again. There was another public announcement. I suppose one of the most frightening things is an incident that happened in southern California about 2 months ago. A laboratory was busted and the individual running it, an illicit lab, had in his possession a do-it-yourself 15 step for the lay person formula, a xerox, so apparently he bought it on the street, of how to make MPPP. That is the one that, unless you make it perfectly, you will get MPTP always.

Senator CHILES. Just making it, you will absorb it?

Dr. LANGSTON. If you try to make the Demerol analog, you will get some MPTP. You can absorb it. But what scares me the most is basically the formula is being sold on the streets to lay people and even a good chemist will get some MPTP. If we get amateur chemists using a xerox formula, God knows what will happen. Ironically, at the bottom of the xerox it says, warning, if made improperly or carelessly, this can damage your clients. See attached and they had a paper on Parkinson's attached. So they know.

Senator CHILES. Good people, they put a little warning on it.

Dr. LANGSTON. Surgeon General approach.

Senator CHILES. Caution: This may be dangerous to your health. You mentioned another patient with symptoms of Huntington's chorea. Would you explain this, what is involved here?

Dr. LANGSTON. We are already aware of several new Demerol analogs. Dr. Henderson talked about the fentanyl analogs. We saw a patient about 6 months ago who used a synthetic, bought from the same person that sold MPTP, took it home and used it. One hour later he started jerking, and his arms, legs, and face, began twitching. This man was a carpenter and obviously completely disabled. Examining him as a neurologist, I could not distinguish his condition from an early Huntington's chorea patient. That is a disease that eventually causes death, and is marked by constant jumping or jerking of the limbs. He clearly used one of these new synthetics. It is permanent.

We think what happened is someone was trying to make a designer variant on MPPP, got other toxic products, and we may have seen the second example of nervous system damage, permanent and disabling from one of these designer drugs.

YOUNG PEOPLE BEING TURNED INTO ZOMBIES

Senator CHILES. Literally, as people are playing with these designer drugs and making these analogs up, they are creating Frankensteins.

Dr. LANGSTON. It would not be an overstatement to say they are turning young people into zombies and it is permanent.

Senator CHILES. If you could speak to all of the young people today walking the streets of California or in Florida who may be interested to experiment in what they read in a glorified way as to some kind of heroin or cocaine that gives you a nice high or lift, what would you tell them?

Dr. LANGSTON. If you could see one of these patients and what it has done to their bodies and their lives, you would never touch a narcotic. It has ruined their lives. Imagine never being able to move normally. Never being able to raise your arm. Never being able to walk to the dinner table. Your life permanently and forever changed. That is what it does.

Senator CHILES. You mentioned that one of these young men had to be disengaged because he had his arm around his girlfriend. He will not have much in the way of a relationship ever again.

Dr. LANGSTON. No, no, never again. Jobs, social relationships—it is full nursing care for some of these patients now. The young woman I showed you, her sister, mother and family spend all day taking care of her. She cannot function by herself.

Senator CHILES. Who is paying the cost for this?

Dr. LANGSTON. We have received some money for the State of California. Robert Roberton and the Drug Abuse Program have helped us. We have received a grant from the United Parkinson Foundation. We are using some money out of that. Medicare and Medi-cal, a county hospital, but it is obviously way insufficient.

These patients require a great deal of care. We are trying to get a grant—we are applying for grants to help to raise money to take care of them.

Senator CHILES. You heard me talking at the start of the hearing and asking questions of Gary Henderson about how we put together a coordinated approach and who should be in charge of doing that. How do you see that meshing together? What advice could you give us?

Dr. LANGSTON. I talked to a lot of people and including some leading scientists around the world. I was just in England——

PROBLEM IS INTERNATIONAL

Senator CHILES. That is interesting because what we are dealing with is an international problem. We don't have any license on this.

Dr. LANGSTON. This is a great deal of concern about this in England.

I think it is an extremely complex issue. If it wasn't, it would have been solved. My suggestion would be to take some of the best minds from around the scientific community, law makers and the pharmaceutical industry, get them together to look at all of the aspects to try to come up with a detailed program all the way from street monitoring to legal control.

It is interesting. If you think what these designer chemists are doing, it is just what the pharmaceutical industry has been doing regarding patent law. A chemical is patented. And another company wants it and they will make analogs so they can sell it as a similar product without infringing on the patent. The drug industry has a great deal of experience. I think they should be involved in helping with this issue as well.

That is where I would start. There are so many complexities when you try to control broad categories. You can inhibit legitimate research. People who had something they thought was legal could be arrested. It is a complex issue and that is why it is such a difficult one.

Senator CHILES. We thank you for your testimony and the work you are doing in this field. We appreciate that.

[The prepared statement of Dr. Langston follows:]

THE DANGERS OF THE DESIGNER DRUG PHENOMENON

PREPARED FOR PRESENTATION TO THE SENATE BUDGET COMMITTEE

JULY 18, 1985

by
J. William Langston, M.D.
Chairman, Department of Neurology
Santa Clara Valley Medical Center, San Jose, California
Assistant Professor of Neurology
Stanford University School of Medicine, Stanford, California

Senator Lawton Chiles, ladies and gentlemen--

I am delighted to be with you today to talk about the designer drug phenomenon. Senator, I commend you for holding this hearing today on this very important topic. There is an overwhelming need on the part of our society to address the many problems caused by the menace and health hazards of illicit drugs of abuse. I believe that by the time I have completed this statement you will understand why I feel so strongly about this issue. It is my hope that, as a result of this presentation, you will understand the origin of my sense for alarm and concern as a physician, researcher, teacher, and parent.

While techniques and methods of control have been developed for many of the well-known street drugs ranging from heroin to PCP, we now have the frightening spectre of seeing the illicit drug market inundated with new synthetic street drugs which can be developed and manufactured faster than they can be identified and controlled. Before describing this further, let me outline the basis for this frightening new development which has been called the "designer drug" phenomenon.

The term "designer drugs" was originally coined in the laboratory of Dr. Gary Henderson at the University of California, Davis. It was originally meant to refer to the increasing sophistication of chemists in illicit laboratories who are now approaching the ability to produce drugs designed to fit the tastes of individual clients. While that is bad enough, this phenomenon has taken a truly pernicious turn as these drugs are now also being tailored to escape the law. Let me explain precisely how this is possible.

The government is required by law to specify the exact chemical structure and name of an individual compound which it wishes to control. There are a variety of reasons why this specificity is required which I will not go into here. Because of the increasing sophistication of these "kitchen" chemists, they are now tailoring these drugs so that they are beyond the reach of the law. It is possible to do this by simply making a minor modification in the chemical structure of a controlled drug such as adding a fluoride or an extra carbon molecule. The new drug, because the alteration is minor, may be expected to have similar psychoactive effects, but because it is no longer exactly the same chemical, it is no longer controlled. Hence, the chemist making this compound is beyond the reach of the law. If a new designer drug becomes widely distributed, the Drug Enforcement Administration can now move to control the compound under emergency scheduling powers, which the agency received in December 1984. These new powers came about in response to the rapid proliferation of designer drugs. Unlike traditional scheduling, which may take from 1 to 2 years to control a substance, an emergency scheduling order may be entered by the DEA Administration.

To give some examples, the amphetamine series (known as "speed" or "crank" on the streets) is estimated to have between two and three thousand potential variations. The fentanyl series is a particularly good example. Fentanyl (known as Sublimaze) is used in approximately 70% of major surgery in the United States. The first designer alteration of fentanyl was alpha-methyl-fentanyl. This drug was considerably more potent than morphine, or fentanyl itself, and was finally controlled in 1981. We are now aware of at least five new variations on the fentanyl series (the most recent are 3-methylfentanyl and sufentanyl). Several of these are estimated to be two to three thousand times more potent than morphine.

Why do they represent such a hazard and public health problem? There are several clear-cut reasons. First, these drugs do not require importation and all the costs and expenses thereby incurred. Secondly, they are much less expensive to make. Thirdly, of course, those making and selling them cannot be prosecuted because they are not illegal. Let me give some examples. It is estimated that a single chemist working an eight hour day could, using the more potent fentanyl derivatives, supply the entire nation's heroin supply on an on-going basis. A single 6 month supply for the United States could be stored in a closet. Hence, one can see the immense attractiveness of this approach in terms of cost and liability to those on the production side of the illicit drug market.

What are the hazards? There are basically three. First, these chemists are obviously not required to carry out safety trials with these new compounds as a legitimate drug company would be. Hence, the first subjects to receive them are not laboratory animals, but human beings using these compounds on the street. Secondly, there are no quality controls in these laboratories as there would be in a legitimate drug company. Hence, contaminants or unwanted compounds are not removed, and probably often not even detected. Thirdly is the issue of potency. The fentanyl variants, for instance, must be cut in microgram amounts. To give an example of how small an amount this is, a postage stamp weighs about 60,000 micrograms. Hence, overdoses are common, and the fentanyl series has been held responsible for at least 100 deaths in California so far. In essence, young drug abusers who take these new synthetics are playing a form of Russian roulette. Only it is not lead bullets that they are aiming at their brains, but chemical ones.

Given this scenario, one would predict it was only a matter of time before a true poison "hit the streets". This is precisely what happened in northern California in 1982, when a highly toxic compound known as MPTP was circulated. This compound is neurotoxic to a group of cells in the brain known as the substantia nigra. By pure coincidence, this happens to be the same area that is damaged in Parkinson's disease. We were shocked to see a group of young adults three years ago come to our hospital (Santa Clara Valley Medical Center) who resembled in every way elderly patients with end-stage Parkinson's disease. These young addicts had literally frozen up overnight, and were totally unable to move or talk. Treatment with anti-parkinsonian therapy was probably life-saving in three; however, these patients continue to be severely disabled and require medication every one to three hours just to be able to move and eat or drink. Two of them have recently undergone prolonged hospitalizations, and the outlook for their futures must be considered grim indeed.

While there are currently only seven severely involved young adults who have been permanently crippled by this first "designer drug disaster", we have now identified an additional 400 people who were exposed to MPTP thinking it was a new "synthetic heroin". My estimate is that we have just been scratching the surface so far, and that there are at least one to two hundred more. Why are these additional individuals important? Because we now have evidence that damage to this area of the brain, even if it is not enough to cause symptoms at first may act like a time bomb, with changes in the brain slowly ticking away. In other words, sooner or later, these young adults could come down with a Parkinson's disease-like state. Up until now, this concern was just theoretical, but in the last several months, we have started seeing a group of young people at Santa Clara Valley Medical Center who used MPTP two year ago who are now starting to develop a myriad of symptoms, all suggestive of early Parkinson's disease in young adults in northern California as a result of this catastrophe. The cost to society, not to mention the human suffering, could be immense.

I bring this entire phenomenon to your attention for a number of reasons. First, I see it as a tremendous potential hazard in terms of dealing with and combating the drug problem among our youth. Ways to deal with this phenomenon and hopefully slow or stop it must be studied now. Secondly, the costs in terms of public health hazard have now for the first time become clear with this first "designer drug" disaster. We need help and assistance in dealing with what may be an onslaught of young people with progressive neurodegenerative disease as a result of this. Further, it seems extremely important to study and try to understand this first catastrophe with the idea of developing techniques and ways to deal with future ones which almost surely will occur given the popularity of this new approach. We have already discovered at least one patient who has an entirely different neurological syndrome characterized by movements closely resembling Huntington's chorea which have completely disabled him. There are also reports that there is a new PCP "designer drug" which is toxic as well. While traditional street drugs pose a major public health problem and need to be dealt with, I believe this is an instance where attention to a developing and potentially even more serious phenomenon is fully warranted now to prevent a much greater problem in the future.

Thank you for your kind attention. My purpose here has been to alert you to the problems inherent in the "designer drug" phenomenon.

Senator **Chiles**. Now we will hear from Randy Rossi, special agent and law enforcement advocate for the California Department of Justice.

I know you are very knowledgeable in the area of designer drugs and you are working with the California legislature to cope with the designer drug problem. We appreciate very much you coming and sharing with us. California has the lead in this and I understand you are working on a law right now. We appreciate your testimony.

STATEMENT OF RANDY ROSSI, SPECIAL AGENT, LAW ENFORCEMENT LEGISLATIVE ADVOCATE, CALIFORNIA DEPARTMENT OF JUSTICE

Mr. **Rossi**. Unfortunately, California has historically been the proving ground for the latest fad in controlled substances. In the 1960's LSD gained its notoriety in the Haight-Ashbury district of San Francisco. In the 1970's phencyclidine, or PCP, was first recognized as a widespread problem among youth gangs in Los Angeles. Now is the 1980's, analogs of the drug fentanyl have spread from southern California.

TESTS FAIL TO SHOW OPIATE

In early 1980, law enforcement officers in California began observing known heroin addicts who exhibited the classic symptoms of heroin abuse, such as scars from injections, constricted pupils, and slurred speech, who confessed to the use of a new drug they called China White. At that time China White was understood to refer to a relatively pure form of heroin originating from the Far East. However, when urine and blood samples from these addicts were tested, the results failed to show any trace of an opiate. This phenomena began in southern California and soon spread up the coast to the San Francisco bay area. The inability to find evidence of traditional opiates was accompanied by a dramatic increase in deaths among addicts associated with this new drug, starting with two deaths in late 1979, and escalating to 49 deaths in 1984 alone.

We have since learned that this drug, the new China White, is not a natural opiate at all. It is a synthetic drug intentionally designed to mimic the effects of a strong opiate. To further complicate matters, we found that we were not dealing with just one drug, but a number of different recipes or analogs of a parent drug called fentanyl. Fentanyl, a schedule II drug, has long been familiar to law enforcement.

Senator **Chiles**. Tell me what you mean by schedule II.

Mr. **Rossi**. To a lay person that refers to a drug that has a medical use but also has an addictive and an abuse potential. Some of your stronger drugs such as morphine and codeine, as well as some of the stronger opiates are in that schedule.

Senator **Chiles**. It would normally be one that you have to have a prescription for but we don't normally think of a schedule II drug as being like a heroin?

Mr. **Rossi**. Yes. Some of the stronger sedatives, some of the drugs that are effective medical drugs but have a high abuse potential.

Senator **Chiles**. What would be schedule I?

Mr. Rossi. Drugs that have no medical use but have a very strong abuse potential, heroin, LSD, some of the other drugs. PCP happens to be in schedule II. It has a veterinary application.

Senator Chiles. No human use?

Mr. Rossi. No.

OVER 150 ANALOGS RECOGNIZED

As of last year, officials in California had actually encountered ten analogs of fentanyl and recognized that over 150, and that is well over 150, potential analogs would be manufactured. California's controlled substance law currently only addresses two of these analogs. Today, most analogs of fentanyl are as legal as table salt despite the fact that 20 percent of narcotic addicts abuse synthetic opiates. The results have been staggering. California is experiencing five to seven known deaths associated with the abuse of these analogs every month. We were thus faced with the difficult decision of whether to individually address each analog of fentanyl as it surfaced on the street, or, in a comprehensive effort, cover the whole family of fentanyl analogs at one time.

This dilemna was not new to California narcotics enforcement. In the case of phencyclidine, we have played cat and mouse with illicit manufacturers for a number of years, addressing each new analog of the drug as it surfaced on the street. From this we have learned that pursuing individual corrective legislation is simply too cumbersome and slow to adequately protect the public.

Senator Chiles. You can't stay ahead of them. Chemists stay ahead of you by making changes?

Mr. Rossi. Absolutely.

Senator Chiles. You have had that experience?

Mr. Rossi. Yes. As of this Monday we heard of a new analog of PCP. We are again playing cat and mouse.

Senator Chiles. And you are always behind.

Mr. Rossi. Yes and the creative manufacturer has an incentive to come up with new analogs.

In November of last year, California Attorney General John Van De Kamp sponsored a comprehensive legislative remedy for the seemingly never-ending list of fentanyl analogs. In January, State Assemblyman William Filante introduced Assemby Bill 2401, which appears before you.

Senator Chiles. Copies of the bill will be placed in the record.[1]

BILL CONTROLS ALL ANALOGS OF PARENT DRUG FENTANYL

Mr. Rossi. This bill controls all analogs of the parent drug fentanyl, distinguishing between schedule II analogs, those that have a legitimate medical use but which may also be abused, and the schedule I analogs, those that have no recognized medical application.

I am happy to report that Assembly bill 2401 is two-thirds of the way through the California legislature, having successfully passed the assembly without a dissenting vote. On Tuesday of this week, it was heard before the Senate Judiciary Committee, where again it was passed with unanimous consent. Assembly bill 2401 is an urgency statute, which means that it will take effect immediately upon receiving the Governor's signature. We anticipate that the bill will be law in California by mid-September.

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[1] See p. 185.

I would like to, if possible, distribute this sample to the chairman. Mr. Chairman, the vial I am distributing to you contains 200 micrograms of a white powder which is a mere speck on the bottom of the vial. 200 micrograms represents a lethal dose of the drug fentanyl. Fentanyl is a lower one-third of all the potential analogs that are available in the fentanyl family.

Senator CHILES. That little speck would be a lethal dose?

Mr. ROSSI. Yes, of a weak family of analog. Our analysis shows it is a little over 10,000 times the strength of morphine. A fatal dose of this analog would be 10 to 20 micrograms. In other words, that vial that you see, that you have before you, would contain 200 street doses of that analog. We are dealing with a very dangerous——

Senator CHILES. Not the full vial but the speck, you could cut that for 200 doses?

Mr. ROSSI. That is correct.

Senator CHILES. If you had the full vial we would be talking about thousands and thousands——

Mr. ROSSI. Hundreds of thousands.

California law enforcement is encouraged that our State legislature has recognized the serious threat posed by fentanyl analogs and its foresight in addressing this problem in an all-encompassing fashion. Mr. Chairman, we have the same enthusiasm and hope for your legislation.

Senator CHILES. Your Assembly bill 2401, what are the penalties?

Mr. ROSSI. The penalties under the act would be the same as manufacturing any of our controlled substances. It would be a felony. I believe it is being bumped up to 3, 5, or 7 years in a State prison.

Senator CHILES. I understand that you are scheduling or listing everything with fentanyl and all of the derivatives. What would keep the chemist from going in and finding a new analog off of these?

Mr. ROSSI. The bill would address all analogs of the drug fentanyl. In the case of PCP or other drugs, the opportunity is absolutely there. We are the number one State in the Nation, unfortunately, for illegal laboratories, our average methamphetamine laboratory can produce $300,000 worth of a product in a week or $15 million worth of a product in a year. We are seizing over 100 of those labs each year. We seized 77 this year so far. The incentive is absolutely tremendous.

Senator CHILES. The thrust of the Attorney General's legislation in the Federal bill is to try to say if it walks like a duck and quacks like a duck it is a duck. In other words, if it has the chemical properties or the health property of the illegal substance, then we classify it so we don't have to use a formula as such on it. Hopefully, if we can get this legislation passed this would give us a way not to deal just with the fentanyl, but the Demerol derivatives and anything else that people can come up with.

ORGANIZED CRIME MAY MOVE IN

Mr. Rossi. You earlier asked about organized crime. In methamphetamines, our number one manufactured drug, organized crime has been making inroads. Organized crime controls California's methamphetamine production. Formulas for fentanyl analogs have been found in several methamphetamine laboratories.

Senator Chiles. You have found fentanyl formulas in the organized labs?

Mr. Rossi. That is correct. We have a fear that this organization is going to move away from methamphetamines and move into the synthetic opiate market.

Senator Chiles. There would be every reason especially if we can't even schedule it as illegal. Again, we run the cat and mouse game. I don't think there is any doubt, but just the question of when would it happen.

We know that your local California law enforcement agencies have knowledge about designer drugs. How do we get that word out to local law enforcement agencies around the country? How do you see us getting that information out? It took you awhile to determine that we are not dealing with heroin. We are dealing with a derivative. How do we get that out?

Mr. Rossi. We ought to have a task force or a central body that other States could go to. I think we need a coordinating agency. As in most controlled substances that originate in California, within a very few years—normally they spread like wildfire throughout our Nation. We have the same fear for this drug.

RESOURCES NOT ADEQUATE

Senator Chiles. Do you think we currently have adequate resources out there to help you or to cope with this problem?

Mr. Rossi. In the State of California, we can investigate only one-third of the leads we have on these laboratories. There are hundreds of laboratories out there. We investigate somewhere around 100 a year, which has been the tradition over the past few years. I feel we could use some manpower and some more expertise for the local law enforcement agencies. We have to have special suits, special equipment that will purify the air before we enter. We are talking about toxic chemicals ranging from the drug of PCP to fentanyl.

Senator Chiles. To go into these laboratories it would be dangerous to personnel themselves without having special clothing?

Mr. Rossi. It has been extremely dangerous. We have already had officers and agents who have been contaminated by different controlled substances we have investigated.

Senator Chiles. Mr. Rossi, we thank you very much for your testimony and for your efforts.

Now we will hear from James T. Moore, director of the Division of Staff Services of the Florida Department of Law Enforcement and Daniel S. Miller, the deputy director of that division.

I would appreciate it if you would discuss Florida's legislation.

STATEMENT OF JAMES T. MOORE, DIRECTOR, DIVISION OF STAFF SERVICES, FLORIDA DEPARTMENT OF LAW ENFORCEMENT; ACCOMPANIED BY DANIEL S. MILLER, DEPUTY DIRECTOR, DIVISION OF STAFF SERVICES, FLORIDA DEPARTMENT OF LAW ENFORCEMENT

Mr. MOORE. It is indeed a pleasure to have the opportunity to appear before you to discuss what we in Florida believe is going to be one of the most epidemic problems, in terms of public health and the economy. We again applaud your efforts in this endeavor.

As you know, in Florida, we have continually been battling with drugs. Our battle has been complicated by both our geography as well as our rapid growth rate. The same geography and environment which promotes our great tourist industry lends itself to facilitating a multibillion dollar illegal drug business in the State.

ORGANIZED CRIME SHOWS MORE CREATIVITY

The joint efforts that we have been involved in with both the Federal and the State efforts have been successful but that very success is one of the factors that is causing the organized crime element to be even more creative and even more sophisticated. As our efforts in the area continue to increase, we are going to see even more creativity and sophistication on the part of the organized crime element.

Even though the concept and phenomenon of designer drugs is not new, increased emphasis is needed in new areas and one is the creativity. In our opinion organized crime's recognition of this easily produced and highly profitable method is and will continue to create a problem for law enforcement both in the State of Florida and across the country.

Thankfully, at this juncture we do not have a serious problem to our knowledge with the concept of designer drugs. However, if we use history as a predicter, the recurrence of these sorts of derivative drugs on the west coast, we are certainly going to have to prepare for the inevitable presence of this phenomenon nationwide.

We think that the efforts you are making are a key in addressing these kinds of problems before they reach epidemic portions. Mr. Chairman, as you know, with your assistance and with the strong support of Governor Graham in the Florida legislature, we did pass legislation this past session which does put the State in a more proactive posture for dealing with this. Most of these efforts have been—they are after the fact. They are oriented toward a problem that has already taken its toll and had its effect. We see that the enforcement effort is only one part of the total solution.

ELIMINATE THE DEMAND FOR DRUGS

As you know, Governor Graham appointed a Council on Drugs and Alcohol Concerns. The number one recommendation of that particular task force was that we really focus on the demand side, on eliminating the demand for all types of drugs, with a special emphasis being placed on education at the local level, education as Mrs. Kidston mentioned earlier, in the youth of the country. With this goal of reducing demand, hopefully over the long term removing the profit motive, hopefully this move will be hampered.

Dan Miller, is here for the State, and he is prepared to address and offer to you his commentary for your consideration.

Senator **CHILES**. Good. I would like to hear from Mr. Miller. If you would stay up here then I will ask questions of both of you.

Mr. **MILLER**. I would like to say I was very impressed by the presentation and actually seeing these individuals. I have read about them in various news articles and literature and seeing it in black and white is very impressive and just adds to my feeling of need to address this terrible problem that I hope will not cover the entire country but probably will.

Senator **CHILES**. I agree with you, Mr. Miller, and I wish we could get the requisite medical, legal and law enforcement officials from all over the country to see this and understand the potential scourge that is out there. Nothing you can read can give you the kind of impact that seeing this film and listening to Mrs. Kidston talk about the actual tragedy can give.

Mr. **MILLER**. With the exception of our extensive drug smuggling problems in Florida, our drug abuse experience has paralleled that of many other States, centering on new and different types of drug being encountered. These drugs are often chemically and pharmacologically similar to but distinct from existing controlled drugs. The clandestine chemist with access to pharmaceutical literature and relatively unsophisticated equipment could with relative ease design new compounds with desired physiological activity that were not illegal. Over the past 15 years a great many of these new noncontrolled designer drugs achieved widespread abuse and were eventually controlled by Federal and State law. It is the growing menace of these drugs that I wish to discuss with you today.

INHERENT DANGERS OF DESIGNER DRUGS

As I mentioned, the concept of designer drugs in not new. However, the term has achieved much recent public and media attention due to alarming encounters of many new, highly potent and dangerous drugs on the west coast. The fentanyl family of drugs have been the most recent. The inherent dangers of such drugs are: No. 1, the lack of pharmacological understanding of the short and long range effects on the use of these new drugs; No. 2, the presence of a potential multitude of impurities and byproducts from sloppy synthesis with unknown toxic effects; No. 3, the high profit potential and ease of manufacture will attract many well financed organized crime opportunists.

Fortunately for Florida, the recent wave of designer drug production has been centered on the west coast. However, given the profit potential it will only be a matter of time before Florida and other areas of the country encounter growing numbers of new dangerous designer drugs. At present only a few dosage form encounters of the fentanyl analogs have occurred in Florida.

We began seeing these a few years ago back in the 1980 to 1981 timeframe when they came on the west coast in the form of China White. In a recent period we have not seen many of these samples at all.

While our medical examiners observe many overdose deaths each year, to date none have, as yet, been definitely attributable to the new wave of designer drugs. These drugs are, however, suspected in a significant number of unexplained deaths but are difficult to detect, that is the drugs themselves are hard to detect, by present scientific methodology.

CONTROL OF NEW DRUGS IS A CONCERN

In recognition of the potential hazards to public safety that the proliferation of such drugs could have in Florida, our Governor's commission on drugs and alcohol, law enforcement agencies and members of our legislature worked together the past year on this problem. Of major concern was our inability to react rapidly to control new drugs as they were encountered. In the past annual legislative action was required to add or make changes to our drug schedules. Through a cooperative effort, the Myers designer drug law was recently enacted to provide an administrative process to control new drugs as they are encountered.

Basically, it provides for the following: One, administrative process whereby the Florida attorney general can by rule add, delete or reschedule any drug to appropriate schedules of the Florida controlled substance law based on actual or potential for abuse.

Senator CHILES. What kind of notice is necessary for that?

Mr. MILLER. The normal administrative procedures act in Florida. The timeframes would apply to that, and normally encompasses 30- to 60-day timeframe to react to the normal process.

It requires that the attorney general consider medical and scientific evaluation by Florida's Departments of Law Enforcement and Professional Regulation as well as any action taken or in progress by the U.S. Attorney General and DEA.

Fortunately, it also provides for temporary emergency action to control any new drugs requiring schedule I status based on a finding of imminent hazard to the public safety.

In that particular case we can react in 1 week to place a new designer drug under control.

Any drug scheduling actions taken remain in effect until June 30 of the following year unless the legislature incorporates these actions as amendments to law.

Some additional problems we see in Florida relative to this problem is that the level and nature of communication and intelligence gathering needs improvement. We need to know better what is going on within our State as well as the Nation. I believe we need to emphasize a central information gathering network——

MANY NOT AWARE OF DESIGNER DRUG PROBLEM

Senator CHILES. How about educating our law enforcement officers at the State and local level about the potential symptoms, and other things, so they could recognize this? Also, our medical people including medical examiners?

Mr. MILLER. A great many of our law enforcement agencies deal daily with the problem, and are really not tuned in and aware of this designer drug problem. Bascially, some consideration needs to be given to that. The crime laboratories and many of the hospital laboratories need to be tuned into a network since they are the first line of defense in detecting these materials so that we can in a coordinated way know what the situation is in Florida as well as around the country and be able to direct our resources to the proper channels.

Another problem deals with—was touched on by earlier speakers, about our lack of reliable and sufficient scientific methodology to properly detect and identify these more highly potent designer drugs such as the fentanyl analogs.

In Florida our problem seems to center around cocaine and the processing of the crude pasteinto the pure cocaine.

Senator CHILES. Have we found the amphetamine laboratories in Florida?

Mr. MILLER. Yes. It is not a pervasive problem.

Senator CHILES. Not to the extent it is in California?

Mr. MILLER. No.

Senator CHILES. Do we know if organized crime has been involved in the cocaine labs?

Mr. MILLER. Very definitely.

In summary, we recognize in Florida that the designer drug wave is coming down the road and we hope through this new law we enacted as well as our efforts to improve intelligence we will be in a better position to react with our resources as this is required.

FLORIDA TRYING TO GET IN FRONT OF PROBLEM

Senator CHILES. I am delighted to hear that Florida is trying to get in front. I hope you will take a look at the California law and also the Attorney General's bill. While I feel that your law is good in terms of recognition, it requires a registration and I think it is going to be hard to stay up with it, as California has found.

Mr. MILLER. We did address this in extensive discussions at our legislative session this year; that is, the process of trying to control classes of compounds.

Senator CHILES. I know in some instances it is hard to get the legislature informed before you've got a problem but I think that's something we need to do in this instance. Hopefully, we can send some copies of this hearing so they will better understand the designer drug problem.

I am glad to hear you say that the wave has not really hit Florida yet. I am glad for that. However, I have to tell you I received a letter from Ronald K. Wright, the chief medical examiner at the University of Miami Medical School.

He says, currently we are investigating the death of a Navy petty officer who seems clearly to have died of an accidental drug overdose. Some of our preliminary tests indicate a derivative of fentanyl and thus we suspect he died of a designer drug. Currently we also have eight other deaths of which we have some suspicion of designer drugs. These shall remain a suspicion for we found levels of other drugs to explain the deaths. Designer drugs, particularly derivatives of fentanyl, are a nightmare for those of us charged with determining the cause of death of people who die suddenly and unexpectedly. The minute amounts capable of producing deaths are very hard to find. Thus, we suspect that more deaths are occurring than are being reported. At any rate, we would appreciate whatever the Federal Government might be able to do to reduce or eliminate designer drugs from this country.

He is the chief medical examiner so it looks like we have one death and we may have others. Again, he points out the great difficulty detecting the drugs and until we get our labs with the sophisticated equipment and with the understanding and looking for the causes, we may have more of a problem than we understand right now. Hopefully we won't have to have a situation like California where we have a rash of overdose deaths or Parkinson-type diseases to get people's attention, not only in Florida but across the country.

I thank you both for your testimony today. I think it is very helpful to us and I am delighted to hear what you have been doing.

This is the first hearing on the designer drug phenomenon. I am hopeful that the Senate Judiciary Committee will move quickly to hold hearings and to consider S. 1437, the Designer Drug Enforcement Act of 1985.

WE ONLY SEE THE TIP OF THE ICEBERG

I have to tell you that as concerned as I was about the question when I began to read about it sometime back and began to move, I had no feeling of the total urgency of the problem that I now have after hearing the testimony today. We have heard the testimony of the Kidstons and the tragedy involving their son as an early experimenter with designer drugs ; Gary Henderson telling us about the phenomenon in California and how it took them a long period of time to determine what was going on; Dr. Langston's graphic demonstration of the film of what has happened to these young people who had no idea what they were getting into and the tragedy that they will have for the rest of their lives which may not be very long; Randy Rossi with the California Department of Law Enforcement tell us about the problems they are facing in California; and Tim Moore and Dan Miller of the Florida Department of Law Enforcement discussing the potential problems in Florida. We are looking at the tip of the iceberg as for as the number of people affected and economic consequences. These phantom chemists are experimenting with human beings and playing with forces that are thousands of times more potent than herion and horrible, which we just saw on film that turned our stomachs. They can blow minds and bodies apart by what they are putting out on the street, understanding that they don't throw anything away—if it is a bad batch they sell it just as quick as the other and the profit potential that is there—with just a few thousand dollars of material bringing billions on the street.

All of this is simply mind-boggling. We are dealing with something that literally can cause havoc in our country and the rest of the world. We need a coordinated effort that can't be just the law enforcement community, it can't be just the Center for Disease Control and the National Institutes of Health, or the counselling service or parents awareness. It has to be all of these and more because Dr. Langston, I think, and Gary Henderson talked about it—we are now in the future drug.

We have heard of all of the potential problems of Dr. Strangelove and the future. To me nothing that I have seen in any of the movies predicting what could happen could be more devastating than some analog that is out there that somebody could be playing with right now. The potential that that little speck in the vial, that I have to have my glasses on to see can have, or that little saucer containing millions of doses—it just makes me understand that this is something that the clock is running on, that we must get on top of now.

Again, I want to thank all of our witnesses for their appearance and for helping us.

[Whereupon, at 11:30 a.m., the hearing was adjourned.]

APPENDIX

[From the Walnut Creek (CA) Contra Costa Times, Oct. 8, 1984]

ALARMED OFFICIALS LINK POTENT SYNTHETIC HEROIN TO DRUG DEATHS

(By Kathleen Maclay)

MARTINEZ.—An incredibly potent synthetic heroin has hit west county streets, alarming law enforcement and drug abuse officials who fear it is linked to an unusually large number of recent overdoses by unsuspecting addicts.

"By the time the addict has the needle in his arm, it's too late," warns Robert J. Roberton, drug division chief for the state Department of Alcohol and Drug Programs in Sacramento.

What makes it too late is phentenal.

That's the name given an ever-expanding group of legal but dangerous chemical compounds manufactured in clandestine laboratories in an attempt to duplicate the original phentenal, a strong anesthetic used in 70 percent of surgeries in the United States.

Chemists involved in this lucrative business, who in a weekend can crank out millions of dollars worth of the drug with the aid of a couple hundred dollars in machinery and supplies, manage to stay one step ahead of federal drug enforcers.

Although phentenal is considered highly addictive and available only with a prescription, slightly different versions of it can be produced that are technically within the law and within reach of drug addicts without prescription, says Roberton.

Haight-Ashbury Free Medical Clinic Director Daryle Inaba contends the law prohibiting the manufacture, use and sale of phentenal was so narrowly written that it applies to two versions of approximately 600 active derivatives.

Phentenal "copies" range up to 6,000 times as strong as heroin, experts say. Their effects are similar to those derived from the opium poppy; a euphoric rush, pupils of the eyes contract, the user experiences a numbing of pain "just like going into surgery," Roberton said.

For most addicts, accustomed to injecting a drug product with only a trace amount of heroin, the added strength can be deadly.

A few micrograms, a dose smaller than a speck of dust, can get an addict high on phentenal. It is considered lethal at just 200 micrograms, making it much stronger than heroin, morphine or LSD.

"To cut it (mix it with other chemicals or substances to dilute its strength) so it won't kill people is quite a problem," according to Roberton, who says he's never seen anything like phentenal in 30 years of drug abuse work.

"Manufacturers aren't worried about quality control and they don't send flowers when somebody dies," he notes wryly.

Associate professor of toxicology and pharmacology, Dr. Gary Henderson of the University of California at Davis Medical School, has contracted with the state for the past three years to analyze blood, tissue and urine samples from suspected drug users and overdoses, in an effort to keep track of what he calls one of the most potent compounds ever known.

His contract was doubled last week, boosting it to about $65,000 and allowing Henderson to hire an assistant to help until the contract expires in April 1985.

"Unless you look for it, you won't see it," said the only man in California with a lab equipped to detect this dangerous "designer drug."

Since 1980, Henderson has linked various versions of the compound to 50 overdose deaths. He has received about 500 samples, some of which related to the same fatalities. Of those 14 were recorded in 1984 and nine of them in August. All nine were in the Bay Area.

"This last month it has really changed," said Henderson.

Sgt. Ray Rodriguez of the Sheriff's Department narcotics bureau says his office and Richmond police recorded five and eight drug overdoses, respectively, in one September weekend. In each of the non-fatal incidents, phentenal was suspected.

Although Henderson has been examining bodily fluid and tissue samples in search of phentenal for several years, he says law enforcement and other officials are inadequately aware of his free tests.

Everyone contacted by the Times said they probably haven't been knowledgeable or tenacious enough reviewing drug overdoses that may have involved phentenal.

Henderson refers to it as an "ostrich with its head in the sand" situation. He started lobbying for a study of the problem when it first was used to drug race horses; he spent his own time and money looking into it for years before persuading the state to step in.

"In overall honesty, we haven't been looking that hard," conceded Inaba, saying they do routine urine tests but fail to send samples to Henderson.

Rod Libbey, Contra Costa's drug programs chief, said the Richmond methadone clinic reports the drug has become a problem with its clients whose tests come back clean when they are obviously high.

Libby said addicts complain that heroin has become harder to find in the Richmond area particularly, forcing them to shop in Oakland or buy what some suspect is phentenal on neighborhood streets. Phentenal has become a "real specific trend on the streets right now."

Henderson said his samples show most phentenal activity in suburban areas of Northern California, rather than ghettos or cities.

"My god, this is a drug of the suburbs," he says, quickly cautioning that the higher incidence of phentenal deaths in smaller towns may reflect the presence of "relatively novice addicts" with weak drug habits.

"For the first time, they've gotten their money's worth," Henderson observed.

"People have no idea what they're taking," Henderson said.

"He's going to shoot whatever is given to him," Roberton agreed.

Roberton hopes to launch a massive publicity campaign in the Bay Area this winter that will do for phentenal what extensive advertising did for the drug PCP and the disease AIDS: "contain" the problem.

[From the Dallas (TX) Morning News, May 12, 1985]

AUTHORITIES FEAR NATIONWIDE SPREAD OF "DESIGNER DRUGS"—CALIFORNIA BATTLES LEGAL STREET DRUGS THAT PACK MANY TIMES HEROIN'S PUNCH

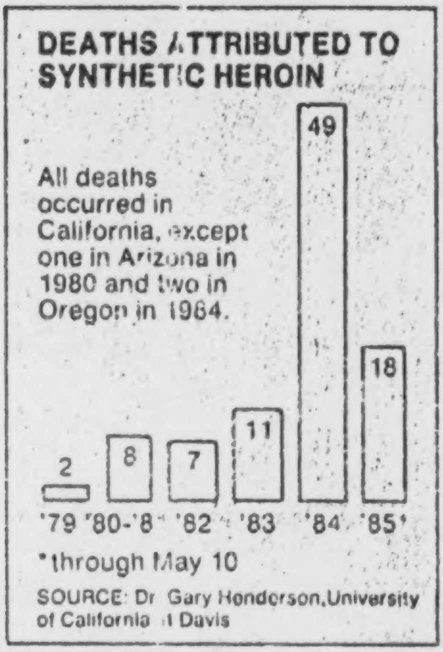
(By Pat Gordon)

Police in California are struggling vainly against a new wave of street drugs: synthetic narcotics that mimic the effects of heroin—but are perfectly legal. And they say it's only a matter of time before the new "designer drugs" make inroads elsewhere in the nation.

"It's a new era in drugs," said Robert Roberton, head of California's division of drug programs. "If it continues, it will replace heroin."

Most designer drugs, of which synthetic heroin is only one, are almost identical to drugs that cannot legally be sold on the streets. Synthetic heroin and Ecstasy, a stimulant and hallucinogen, are the two most widely abused. The designer variations are legal because drug laws define each illegal drug by its molecular structure. By making even minor changes in the structure, a chemist can bylass the law.

But officials say that is only one reason designer drugs are attractive to manufacturers—and a nightmare to police. Synthetic heroin, for instance, mimics the effect and physical appearance of the real thing but is considerably stronger. The raw materials, which are needed only in very small quantities, are cheap, readily available and hard to trace.



DEATHS ATTRIBUTED TO SYNTHETIC HEROIN

All deaths occurred in California, except one in Arizona in 1980 and two in Oregon in 1984.

*through May 10

SOURCE: Dr Gary Henderson, University of California at Davis

The finished product is nearly impossible to detect or analyze except with the most sophisticated laboratory equipment. The chemist can change the drug much faster than lawmakers can change the law, and the possible variations may be almost endless.

"Why bother with Customs or crop failures when for a couple of hundred dollars and two weeks' work you can turn out enough synthetic heroin to supply the entire U.S. heroin population for six months?" asked Roberton.

"This is the wave of the future," said Gary Henderson, a professor of pharmacology at the University of California at Davis. "You haven't seen anything yet."

Synthetic heroin was unknown to authorities until Dec. 28, 1979. Then, within two hours, two men arrived dead at Anaheim Memorial Hospital near Los Angeles. Heroin paraphernalia had been found near each victim, but autopsies showed no traces of narcotics in their bodies. By mid-1980, eight more addicts had died without leaving a clue as to what had killed them.

"We were desperately trying to determine the cause of their deaths," recalled Robert Cravey, head of forensic toxicology for Orange County. "We weren't seeing anything. . . It never occurred to us to look for something so potent that the amounts would be so small as to escape us."

It took Drug Enforcement Administration chemists Donald Cooper and Andrew Allen more than three months to identify the killer drug as alpha-methyl fentanyl—a variation of an anesthetic commonly used during surgery. Since then, a total of 10 fentanyl analogs have hit the streets and 85 more addicts have died of fentanyl overdoses. The substitutes, which can be 3,000 times as strong as heroin, are so potent that chemists must look for one part per billion to detect them, Henderson said.

Unable to prosecute the manufacturer even if they found him, California police have watched helplessly as the use of synthetic heroin has spread. Today, fentanyl analogs are used by an estimated 20 percent of the state's 100,000 heroin addicts, Roberton said.

A study conducted by a clinic for heroin addicts in Marin County, north of San Francisco, showed that 65 percent of its clients were addicted to fentanyl, said director Brian Slattery.

Heroin these days isn't heroin at all," said Nika St. Clair, director of another northern California clinic. "It's a synthetic."

Although the problem is growing, deaths from fentanyl remain relatively rare compared to deaths from heroin, which killed 390 California addicts in 1982–83, the latest year for which figures are available.

Experienced addicts aren't dying from fentanyl overdoses, Henderson said; most victims are people who stop using heroin for a while and then begin again. No longer having a high tolerance for heroin, those returning to the drug end up overdosing with the stronger synthetic variety, he said.

However, fentanyl isn't the only synthetic heroin on the market, and it isn't the only one causing severe problems.

Authorities say that as many as 300 addicts may eventually contract Parkinson's disease because they injected a defective dose of MPPP, a legal Demerol analog that is also a synthetic heroin. Since 1982, seven addicts in the San Jose, Calif., area have contracted the illness, which causes tremors and paralysis.

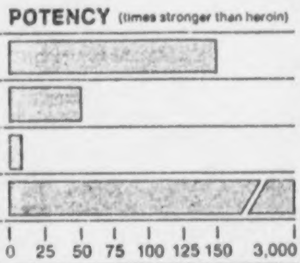
Physicians issued a warning to the heroin community, and the faulty MPPP vanished from the streets.

Officials believe the contaminated drugs may have been manufactured by a man who was arrested in Brownsville, Texas, in October. In the clandestine lab of 50-year-old San Jose attorney Roberto Calunga Garza—who pleaded guilty to charges of manufacturing, distributing and possessing PCP ("angel dust")—authorities found illegal drugs as well as defective MPPP.

California has started a program through which addicts can anonymously send in samples of heroin for a free analysis. The program has met with limited success, said Ian Irwin, a chemist at the Institute for Medical Research, because addicts are reluctant to part with a dose.

MOST COMMON FORMS OF SYNTHETIC HEROIN

	First seen by DEA	Date controlled	Last seen by officials
Alpha-methyl fentanyl	Orange County, Calif., 1979	Sept. 22, 1981	1981
Para-fluoro fentanyl	Los Angeles area, 1981	Not controlled	1982
Alpha-methyl acetylfentanyl	San Francisco area, 1982	Not controlled	1984
3-methyl fentanyl	San Francisco area, 1984	April 25, 1985	Still on the streets



SOURCE: Drug Enforcement Administration; Dr. Gary Henderson, University of California at Davis.

The Dallas Morning News

"When we look at the samples, we get a sense of what designer drugs are available," Irwin said. "We've already found a new Demerol analog."

For now, authorities are concentrating most of their efforts on locating the maker and distributors of the fentanyl analogs and getting those analogs classified as controlled substances. Neither is an easy task.

Police say they are convinced they are not dealing with a typical garage chemist, someone who found a recipe for synthetic heroin in an underground cookbook. Of the 10 fentanyl analogs analyzed by DEA chemists, two have never been reported in chemistry literature, Cooper said. And the formulas that have been writtern up are not easy to find—or understand—he said.

The consensus among police is that one chemist or at least one group of chemists is responsible for making all the analogs.

Henderson, an expert on the fentanyl family who was hired by the state to analyze synthetic heroin and monitor its use, describes his unknown adversary as "world class . . . a mysterious genius . . . probably a chemist by profession."

Pure fentanyl is to toxic that an amateur "wouldn't be able to make it without killing himself," he said. (Which also means that unless the police who eventually discovered the lab known in advance what is being made there, they could poison themselves while handling the drug.)

"It's like baking a cake," said Frank Sapienza, a DEA chenist in Washington, D.C. "You can follow a recipe or, if you're good enough, make up your own. These guys know enough chemistry to make it up."

"He (the manufacturer) has got a chemistry background," Cooper speculated. "I would guess a graduate student."

Drug enforcement agents say finding the fentanyl lab will be extremely difficult. Most clandestine labs are discovered because the operator buys large quantities of chemicals or because neighbors report foul smells, said DEA chemist Bob Sager.

"With this stuff, you're talking about buying a pint, instead of a drum, of chemicals," he said. "The operator could even take what he needs from a well-stock chemical lab and nobody would miss it. . . . There is also little odor."

According to chemists, the formulas for about 200 fentanyl analogs are known, but the possibilities are endless. When one analog is put on the controlled substances list, it mysteriously disappears from the streets, and soon afterward a new variety replaces it, Cooper said.

"The crooks are out there getting around the law and laughing at our efforts to do anything about it," said Peter Evans, Marin County deputy district attorney.

So far, fentanyl and four of its analogs are on the federal controlled substances list. Until last year, it took the Drug Enforcement Administration about two years to get a compound added to the list. In 1984, Congress approved emergency scheduling, which allows DEA to make a compound a controlled substance within about 30 days.

In California, only fentanyl and two of its analogs are controlled. But a bill recently introduced in the Legislature would place the entire fentanyl family on the list, said Randy Rossi, a lobbyist for the state attorney general's office.

DEA officials have toyed with proposing such a federal "umbrella" law, but discarded the idea because of expected opposition from pharmaceutical companies and problems in drafting the law.

"Researchers say we have too many controls on drugs already," Sapienza said. "And it would be difficult to make a law broad enough to include everything, yet narrow enough to define it. We're hoping that emergency scheduling will take care of the problem."

And even if the California Legislature passes a state umbrella law prosecutors worry how well it will stand up in court.

"It will be hard to pass a law making something illegal that doesn't even exist," Evans said.

If the trend toward synthetic heroin continues, authorities said, it will change the way they attack the heroin trade. Traditionally, police have concentrated on controlling the importation of heroin from Asia, South America and Mexico. Locally manufactured compounds, however, would pull authorities away from customs points and border patrols to search for labs at home.

"In some respects, fentanyl would be better," said Lt. Alan Johnson, head of a San Mateo County drug task force. "There's nothing I can do about a Mexican heroin lab, but if I knew where an (illegal) fentanyl lab was, I could move against it."

For now, the synthetic heroins appear to be confined to California, with only isolated doses showing up in other states, federal drug official said. However, they said the likelihood that it will continue to be a West Coast problem is remote.

"I'm afraid it will spread," Cooper said. "As more people become aware that it will give the same effect as heroin, they'll be willing to substitute it. Then a market will be created."

While officials are uncertain why the synthetics have failed to sweep other areas of the country, they have theories. DEA deputy assistant administrator Gene Haislip believes adverse publicity about its toxicity and a lack of distributors has helped to slow fentanyl's spread. Even in California, synthetic heroin is more readily available in rural and suburban areas than in the cities, officials said.

"The whole key is in selling it," Henderson said. "It's not being distributed by the mainstream, which would make sense if you were new (in the heroin trade) and didn't want to take on organized crime."

Other officials said a heroin shortage in California has created a market that may not yet exist in states with a flourishing heroin trade. Still others say the market may exist in other states, but the technology to manufacture fentanyl analogs doesn't.

But even though synthetic heroin hasn't flooded the nation, the potential is definitely there, officials said.

"It's serious," Haislip said. "And it's showing rapid growth."

[From the New York Times, Mar. 24, 1985]

CALIFORNIA ADDICTS USE LEGAL, SYNTHETIC NARCOTICS

(By Sandra Blakeslee)

LOS ANGELES, March 23—One or more chemists working in secret California laboratories are turning out synthetic versions of heroin and cocaine that addicts say are indistinguishable from the naturally derived drugs.

Although not easy to fabricate, the synthetic narcotics are legal to possess or manufacture. Illegal drugs are defined by exact chemical formulas, and the new synthetics have slightly different formulas.

Further, the synthetic drugs are stronger and potentially more lethal than the narcotics made from natural sources. In the last four years, there have been 90 confirmed deaths from synthetic heroin, 87 of them in California, said Chauncey Veatch, director of the California Department of Alcohol and Drug Programs. But statistics are limited, he said, describing those deaths as "just the tip of the iceberg."

HUGE PROFITS POSSIBLE

The synthetic heroin, which is just as addictive as natural heroin, is so potent, according to drug authorities in California, that one chemist working an eight-hour day could supply the nation's daily heroin demand. An investment of $1,500 in equipment could reap millions of dollars in profit, they say.

According to Dr. Robert J. Roberton, chief of California's Division of Drugs, 20 percent of the heroin now used in the state is synthetic. Users of synthetic cocaine are just beginning to appear for treatment in clinics.

These narcotics are the newest manifestation of a trend toward more sophisticated production of synthetic drugs, Dr. Roberton said. The chemistry has been known for decades and is straightforward.

The pain-killing morphine molecule, for example, can be shaped into thousands of configurations by tacking on or snipping off groups of atoms. The result is still basically morphine, but the potency, length of action, euphoric effects and toxicity can be different.

Chemists employed by pharmaceutical companies do this kind of manipulation all the time. They often try to make slightly different versions of successful drugs made by their own or competitors' concerns. University research scientists also synthesize molecules and publish detailed steps in the scientific literature. But when legitimate drug chemists create new compounds, they painstakingly test them on animals, sometimes for years.

Synthetic versions of many easy-to-make street drugs, such as amphetamines and hallucinogens, have been around since the 1970's, Dr. Roberton said. But now some college-educated chemists have begun designing versions of narcotics usually derived from plant sources.

The increasing use of cocaine by wealthy Americans, he said, has led to an increased use of heroin, which counteracts the irritability resulting from chronic cocaine use.

All the experts agree that the problem thus far is mostly confined to California but that the potential for its spread nationwide is real.

APPEAL IS VARIED

The synthetic drugs appeal to some addicts for a variety of reasons, Dr. Roberton said. The synthetics cost the same as natural drugs, and some people say they seem more potent, he said. Other addicts believe the synthetic drugs are less adulterated, and therefore less dangerous.

Still others, Dr. Roberton said, simply ask for "China White," the name under which pure heroin is sold, and are unaware that they are getting a synthetic version.

The Federal Drug Enforcement Administration is trying to catch up with those who are producing the synthetic drugs. The comprehensive crime bill enacted in October allows the Government, on an emergency basis, to outlaw a particular illicit drug variant in 30 days, said Ron Buzzeo of the agency's Office of Diversion Control. It used to take more than a year.

Experts can only guess at how many of these chemists are operating in California. Some authorities, like Dr. Roberton, say that the synthetic drugs are the product of one mastermind. Others, like Dr. William Langston of the Santa Clara Valley Medical Center, in San Jose, said he thought there might be three or four laboratories concocting the new drugs.

In any case, organized crime does not seem to be involved in synthetic narcotics, Dr. Roberton said.

VARIANTS DATE FROM 1980

The first narcotic molecule to be altered by underground chemists was fentanyl, widely used as an anesthetic for prolonged surgery. It has hundreds of variants, one of which is used by gamekeepers to immobilize large wildlife.

In 1980, one variant, alpha-methyl-fentanyl, was first seen on the streets, said Darryl Inaba, treatment director at the Haight-Ashbury clinic for drug abuse in San Francisco. The clandestine chemists "mistakenly believed its potency was the same as fentanyl," he said, but it turned out to be 1,000 times as potent. At least 20 people died from overdoses, and a year later the Drug Enforcement Agency put alpha-methyl-fentanyl on the list of controlled substances.

In 1982 another California chemist produced a variant of Demerol, a synthetic narcotic used by doctors to dull pain. The new molecule, methyl-phenyl-propionoxy-piperidine, or MPPP, is structurally identical with Demerol, except that one carbon and one oxygen atom are switched.

Addicts say MPPP produces effects like heroin, said Dr. Paul Garbe of the Centers for Disease Control in Atlanta. But sometimes the drug left them disoriented.

This was a result of an extra molecule accidentally created in the synthesis of MPPP, said Dr. Langston of the Santa Clara Valley Medical Center.

Two addicts who injected themselves with the contaminated drug literally "froze" with a needle stuck in the arms, Dr. Langston said. The molecule destroyed cells in an area of the brain controlling movement. Seven addicts in their 20's or 30's exhibit the profound loss of motor control symptomatic of advanced Parkinson's disease, Dr. Langston said.

Two years ago a new variant of fentanyl, tri-methyl-fentanyl, appeared on the streets. It is 3,000 times as potent as heroin, said Dr. Roberton of the California drug agency. "You could kill 50 people with the amount that fits on the head of a pin," he said.

If the synthetic narcotic is not diluted a hundredfold, Dr. Roberton said, a user could easily take an overdose. "I believe novice users are dying from it," he said.

But its strength is also a selling point for synthetic drug consumers. Because it works in such small amounts, tri-methyl-fentanyl does not show up in routine urine tests such as those given prisoners, Dr. Roberton said. An amount the size of a postage stamp, smuggled into a prison, is enough for several hundred inmates.

A new version of fentanyl has just arrived in Haight-Ashbury, supposedly several thousand times stronger than heroin, Dr. Inaba said. Its effects last 24 hours. Of two people who used it, one is being treated at the clinic. The other is dead.

[From the Chicago Tribune, Apr. 21, 1985]

CHEAP, LEGAL, DEADLY: "DESIGNER DRUGS" A FRIGHTENING TREND

(By Jeff Leen)

The drug, 1,000 times more powerful than heroin, is designed in a clandestine lab by a renegade chemist, a brilliant phantom who has earned the grudging respect of law enforcement pharmacologists.

It is cut innumerable times and passed off as Persian White, the caviar of heroin. It is sold in the redwood suburbs north of San Francisco to chic young professionals, junkies in hot tubs.

It killed 49 people last year. It is cheap, addictive and perfectly legal.

By tinkering with the molecular structure of fentanyl, a synthetic painkiller routinely used in surgery, the unknown chemist has created the latest fad to come out of California—"designer" heroin.

"We're talking about a world-class medicinal chemist," said Dr. Gary Henderson, a pharmacologist at the University of Calfironia at Davis who coined the term "designer drugs" for the synthetic substances that began cropping up on the West Coast in the late '70s.

"First they said it was California craziness, 'It's gong to go away.' I don't see it. Something that's 1,000 times more powerful than heroin, dirt cheap to make, hard to detect, you can smoke it, snort it, you don't have to inject it . . ."

The state-of-the-art drug poses unique problems. Coroners cannot detect it in overdose victims. And there is a laboratory loophole that could endlessly frustrate the law:

New variations can be turned out faster than they can be identified and outlawed. And when they are finally made illegal, a sophisticated "designer" can create a new, legal drug merely by altering the molecule. The users are the guinea pigs.

"This is very, very frightening," said Chauncey Veatch, director of the California Department of Alcohol and Drug Programs, which expects 78 people to die this year from designer drug overdoses.

To date, 90 people have died from such overdoese, 13 this year. The fear is that the new heroin will sweep the country. Three designer drug deaths have occurred outside California, two in Oregon and one in Arizona.

"As California goes so goes the rest of the nation. That's what happened with LSD," warned Frank Chellino U.S. Drug Enforcement Administration spokesman in Miami.

Last month, Sen. Lawton Chiles [D., Fla.] proposed legislation that would focus federal attention on the problem.

"This will come out of California and, look out, it'll come across fast," Chiles said. "It's so easy to produce these drugs in small labs: A $500 investment on chemicals can produce a $2 million batch of synthetic heroin. There's just too much money there. It's just go to spread."

Henderson said he has heard that underground chemists are coming to California to learn how to make fentanyl.

Right now, law enforcement can do little. If DEA agents raided a designer drug lab tomorrow, chances are they couldn't make any arrests.

"I think [arrests would be] very doubtful," said Gene Haislip director of the DEA's office of diversion control.

It used to take months, even years, to list a drug—by chemical formula—in the Controlled Substances Act. "We can't take action based on a suspicion. We have to have data," Haislip said. Now, under legislation passed last year, a drug can be made illegal in 30 days.

"We're hoping this new authority will enable us to nip this in the bud and keep this from spreading," Haislip said. "But I can't say that it will."

Thirty days provide plenty of time for a smart designer to change the formula.

So far, DEA chemists have uncovered 10 varieties of fentanyl. Only two are illegal, and two more are scheduled to be outlawed soon. The newest and deadliest, 3-methyl-fentanyl, becomes illegal April 28.

"We believe it is the one connected with the deaths in California," Haislip said.

Once 3-methyl-fentanyl is outlawed, there are plenty of others waiting in the lab. Chemists have created 200 more variations of fentanyl in industrial laboratories. The variations could go as high as 1,000.

"If you have yourself boxed in where you have to have the formula, it looks like those fellows can always stay ahead of you," Chiles said. "They're going to have to change the definition of the crime."

Chiles' proposal would direct the government to include designer drugs in a strategy plan scheduled for release in July. The senator also wants the congressional Office of Technology Assessment to study the drugs and find out what the government is up against.

From LSD in the 1960s to PCP in the 1970s, chemists have long tinkered with illicit substances to thwart the law and produce tailor-made effects. The most famous designer was Augustus Owsley Stanley III, who manufactured high-grade LSD in the Haight-Ashbury of the mid-1960s. Owsley, as he was known, was finally arrested in 1967. He was last seen making jewelry in rural Australia.

Fentanyl was developed in the early 1960s by Janssen Pharmaceuticals, a Belgian firm. In its pure form, the drug is a short-lasting analgesic 100 times more powerful than morphine. Marketed as Sublimaze, it was introduced in 1968 to the United States, where it is now used in 70 to 80 percent of surgical operations.

"It's a very, very important drug clinically," Henderson said. "It ranks up there with the top five drugs in the world."

In the late 1970s, race track veterinarians noticed that thoroughbreds were being doped with fentanyl so they would run faster.

At the same time, fentanyl derivatives began appearing in California as "China White," a high-grade Southeast Asian heroin. California, home of 20 percent of the nation's heroin addicts, was ripe for the drug. It took more than a year to outlaw synthetic China White.

About one-fifth of California's addicts are now using fentanyls. Many think they are taking powerful heroin, but users increasingly ask for synthetics.

"The word on the street about the analogs is they're much more potent than heroin and they seem to last longer," said Darryl Inaba, who runs the Haight-Ashbury Drug Detox Project in San Francisco.

Otherwise, the high is identical to heroin's, and the drug is just as addictive.

"Sometimes people will swear that it's heroin, they bought it from a dealer they've known for years, he just got off the plane from Bangkok," said Henderson. "The dealers don't know what they're selling, and people don't know what they're buying and using."

The first known overdose was in December, 1979. Soon, the deaths were happening at the rate of 8 to 10 a year.

Then in 1983, 3-methyl-fentanyl appeared on the street as Persian White, the world's finest heroin. It cost as much as $350 a dose. It was 1,000 times more powerful than heroin. Forty-nine people overdosed in California, more than had died from synthetic heroin in all the previous years combined.

"This is sort of your basic street research for profit with indifference about what happens to people," the DEA's Haislip said.

Many of the dead were from California's new class of upscale junkies, who use heorin to temper the effects of cocaine. "The distribution pattern is very curious," Henderson said. "It breaks all stereotypes. It's distributed essentially in the suburbs of California. We've never had an overdose case in Los Angeles.

"We find it in small farming communities in California. If somebody wanted to buy it, I'd tell them not to go to ghettos in Los Angeles or San Francisco, because you're not going to find it there."

In the Bay Area, "the people are coming from Marin County," said clinic director Inaba. Most often, they're white, upper middle class, educated, he said.

And dumb about drugs.

"It's new or naive users who are succumbing to the drugs," Henderson said. "They're just buying something that's powerful, and [the overdoses] probably would occur if they were buying high-grade heroin."

The synthetics are so deadly because they are so potent. A street dose contains only an infinitesimal speck—about 50 micrograms, an amount that could be hidden on the head of a pin.

"You could take any of the street samples and send it to a laboratory and they would send it back as food-grade lactose or powdered sugar," Henderson said. "It's 99.9 percent purce sugar or lactose."

Because the concentrations were minute, medical examiners were baffled by the early deaths. Then, in January, 1981, DEA chemists Don Cooper and Andrew Allen identified the first synthetic China White.

"On the sample I received for the original analysis, the laboratory that submitted it said this powder is supposedly killing people but we can't find anything in it," Cooper said from the DEA laboratory in Tysons Corner, Va.

Such "fantastically small amounts" can be detected only by the most sophisticated labs, said Henderson, who developed the first screening test for the drugs.

"The concentrations we're seeing in the blood are parts per billion and parts per trillion," he said.

Drug agents estimate that a single chemist in eight hours could supply the nation's heroin demand for a day. A closetfull of the drug could feed the nation's addicts for six months.

Henderson speculates that the supply is now coming from "one maybe two, very sophisticated labs." Working for two weeks at a time, the labs can produce about 200 grams, enough for 4 million doses. The four or five raw materials, also available on the market, cost "a couple hundred dollars."

DEA chemist Cooper believes the drugs are the work of one man, perhaps a brilliant graduate student. Henderson agrees: "He's the Owsley of the '80s."

Cooper speaks admiringly of the "nifty little variations," the sophistication of the syntheses, the uniformity of cutting materials that are "mixed very nicely, no hot spots." A hot spot—a lump of pure material in the mix—could kill.

"Somebody's taking great care to do the job right," Cooper said.

The new Owsley is working amid a West Coast designer drug renaissance.

"The drugs can be designed to produce the effect you want," Henderson said. LSD is still plentiful, and quality control "is very good." Some designers are making amphetamine-mescaline hybrids, for "people who want to use a psychedelic drug but don't have a lot of time to spare."

Overdose isn't the only risk, however.

The first designer drug disaster occurred in 1982. A group of underground chemists in northern California tried to design a copy of Demerol, a narcotic painkiller less powerful than heroin or morphine. They came up with MPPP. In their batch was a byproduct with a side effect: Parkinson's Disease, a chronic nerve affliction.

"These young addicts had literally frozen up overnight and were totally unable to move or talk," said Veatch, the head of California's drug program.

Twenty people were permanently crippled, and 500 more may eventually develop the disease.

"Most of the people we talked to thought they were buying heroin," said Dr. Paul Garbe, an epidemiologist at the federal Centers for Disease Control in Atlanta. "These drugs haven't even been tested on animals. Nobody knows what kinds of effects they're going to have on humans."

And nobody knows where the laboratory ingenuity will lead. Henderson believes the answer lies in understanding abusers, not drugs.

"You can play with the structures endlessly," Henderson said. "Once you know the chemistry, there are almost an unlimited number of chemicals out there that could be made and used and abused. Passing laws is not the answer. We could spend the rest of our lives compiling lists of illegal chemicals."

CHEMISTS ARE FASTER THAN THE LAW

(By D. Lowell Jensen)

WASHINGTON.—Drug traffickers and clandestine chemists, in an attempt to avoid prosecution under existing drug laws and to maximize their profits, have developed an ingenious scheme for producing and distributing abusable yet uncontrolled drugs.

Through slight modification of the chemical structure of a controlled substance the chemist can create a new drug which produces the high the user seeks but is not unlawful.

Although the Drug Enforcement Administration can place these substances one by one under the Controlled Substances Act, the process may take several months. By that time, the enterprising chemist may have produced yet another uncontrolled designer drug.

The Drug Enforcement Administration has used every available resource to combat the problem. The first designer drug, China White, was administratively placed under ~~the Con~~trolled Substances Act in 1981, but other, similar drugs took its place.

Realizing the need for quicker control of these drugs, the administration last year requested emergency power to quickly place new drugs on the controlled list. Since October, DEA has used this emergency authority to place the most dangerous and highly abused designer drugs under the Controlled Substances Act.

But despite this new authority and DEA's enforcement actions, individuals continue to evade the law by producing new designer drugs faster than they can be controlled.

In response to this problem, the Department of Justice has submitted to Congress new legislation, which, if enacted, will make it unlawful to manufacture or distribute designer drugs for human comsumption.

The Designer Drug Act of 1985 would provide law enforcement officials with the legal authority to arrest and prosecute those persons who engage in activities involving designer drugs even if the substances are not under the Controlled Substances Act.

The designer drug problem illustrates the increasing complexity and sophistication of drug abuse and trafficking. It is imperative that we continue to use every means at our disposal to attack this problem, including the development of new laws when existing ones are insufficient.

The health and well-being of our country depend on it.

"CHINA WHITE"—SYNTHETIC HEROIN

HISTORICAL BACKGROUND

In December of 1979, the Orange County Coroner investigated two deaths which were thought to be drug-related. The cases appeared to be classic narcotic overdose deaths. The victims were known heroin addicts, syringes and other paraphernalia were found at the scene, and autopsy findings showed pathological changes consistent with opiate poisoning. However, chemical analysis of the paraphernalia, blood and other tissues showed no evidence of narcotics or other drugs of abuse.

In 1980, a total of 12 similar, unexplained narcotic like overdose cases occurred in California and one similar case was reported in Arizona. In California, most of the deaths occurred in Orange and Monterey Counties. A common finding in each case were the victims said to be using "China White," the name given to very pure heroin obtained from Southeast Asia.

During the same period, Drug Enforcement Administration laboratories, as part of their drug surveillance program, analyzed a series of illicit drugs confiscated or purchased on the street and found them to be free of any drug even though they were being offered on the street as narcotics. Again a common finding in these cases was the fact the drugs were sold as "China White."

In January, 1981, the DEA reported the identification of the compound present in "China White" samples as 3-methyl fentanyl. This initial identification was incorrect and subsequent reports from the DEA identified the material as alpha-methyl fentanyl.

In May, 1981, alpha-methyl fentanyl was identified by the DEA in powder samples found in a clandestine laboratory in New Jersey. The laboratory apparently was engaged in the synthesis of phenyl-2-propanone, an intermediate in the synthesis of amphetamine. Phenyl-2-propanone can also be used in the synthesis of alpha-methyl fentanyl (but not fentanyl.) Although this synthetic route has not been reported in the chemical literature, it is probably the best, most efficient way to synthesize alpha-methyl fentanyl.

On September 22, 1981, at the request of the Drug Enforcement Administration, alpha-methyl fentanyl was placed in Schedule 1 of the Federal Controlled Substances Act.

Fairly recently, a new illicit fentanyl derivative was reported by the DEA Special Testing and Research Laboratory in McClean, Virginia. The compound, identified as parafluoro fentanyl, was present at a low concentration in lactose in samples obtained by the Los Angeles Police Department. This compound remains a non-controlled substance at the time of this writing. Most recently, another unnamed analog of fentanyl has been discovered.

PHARMACOLOGY OF FENTANYL-LIKE COMPOUNDS

Dr. G. L. Henderson of the Department of Pharmacology, School of Medicine, University of California, Davis, has conducted extensive research on powder, and blood, urine and tissue samples associated with China White deaths. He has used information from the Janssen Research Laboratories, Beerse, Belgium, detailing analytical standards of a number of fentanyl-like compounds and other unpublished data on the chemistry and biological effects of relevant drugs in the fentanyl series.

The fentanyl family of narcotic analgesics is a nearly limitless series of very potent, easily synthesized compounds. Almost any simple modification of the basic fentanyl structure will yield a potent narcotic. Many of the analogs are several times more potent than fentanyl itself. More importantly, from a drug abuse standpoint, most fentanyl analogs can be easily synthesized from a variety of readily available precursors.

Alpha-methyl fentanyl is a simple analog of the clinically important drug fentanyl. The synthesis and pharmacology of fentanyl was first reported in the patent literature by the Belgian pharmaceutical company Janssen Pharmaceutica in 1965. In 1968, fentanyl was introduced clinically in the United States as an intravenous anesthetic/analgesic agent under the trade name Sublimaze. Fentanyl's potency as an analgesic (80 times that of morphine) its rapid onset (2–3 minutes) and short duration of action (30–60 minutes) have made it an agent of choice for anesthesiologists. At least three other fentanyl analogs, alfentanyl, lofentanyl and sufentanyl will be introduced into clinical medicine in the United States within the next few years.

Alfentanyl is a very short acting analog of fentanyl which will be used to provide surgical analgesia for short (30 minutes or less) gynecological, urological, diagnostic and dental procedures. Lofentanyl is a very long acting, very potent analgesic which will be used when prolonged analgesia and respiratory depression is required, i.e. multiple trauma patients, tetanus, and in intensive care units. Sufentanyl is a very potent (5 to 10 times greater than fentanyl) compound suitable for very painful surgical procedures such as cardia and deep abdominal surgery.

The original patent reported that methyl substitution in the sidechain alpha to the basic nitrogen in the peperidine ring enhanced the analgesic activity. Methyl substitution into the piperidine ring itself will yield potent analgesics. The synthesis and pharmacology of the 3-methyl derivatives of fentanyl was reported by T. N. Rileyt of the University of Mississippi in 1973. These compounds were actually synthesized and studied by Janssen years earlier, but not reported. One particular analog, cis( )3-methyl fentanyl is nearly 7000 times as potent as morphine. However, this derivative is rather difficult to synthesize and, therefore, is unlikely to be an illicit drug.

Until recently, neither fentanyl nor its analogs have been drugs of abuse in man, although fentanyl has been used illicitly for some years as a doping agent for race horses. The drug's pronounced stimulatory effect on horses, its short duration of action, its extreme potency, and the fact that the drug cannot be detected in blood or urine by routine analytical methods make it an ideal doping agent. Likewise, these same features of easy synthesis, extreme potency, and difficult detection by routine analytic methods make the fentanyl analogs ideal drugs of abuse in man.

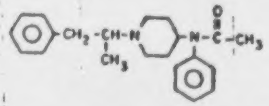
Following is a list of fentanyl related deaths compiled by Dr. Henderson:

Date	Location	Age	Sex
Dec. 28, 1979	Anaheim, CA	30	Male.
Do	do	38	Do.
Jan. 7, 1980	Carmel Valley, CA	26	Female.
Jan. 27, 1980	Santa Ana, CA	38	Male.
Mar. 20, 1980	Tempe, AZ	30	Do.
Mar. 29, 1980	Anaheim, CA	24	Do.
Apr. 6, 1980	Santa Ana, CA	23	Do.
Apr. 27, 1980	Placentia, CA	28	Do.
May 12, 1980	Santa Ana, CA	30	Female.
June 14, 1980	Buena Park, CA	37	Male.
Aug. 4, 1980	Orange, CA	30	Do.
Aug. 10, 1980	Stanton, CA	49	Do.
Nov. 6, 1980	Seaside, CA	28	Do.
Do	do	34	Do.
Dec. 10, 1980	Fort Ord, CA	28	Do.
Mar. 30, 1981	Bakersfield, CA	35	Female.
Jan. 4, 1982	Stockton, CA	20	Male.
Mar. 4, 1982	Fullerton, CA	25	Do.
Aug. 1, 1982	San Diego, CA	28	Do.
Sept. 12, 1982	do	31	Do.
Sept. 18, 1982	do	32	Female

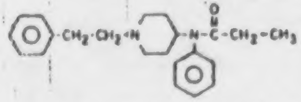
In addition, 11 cases of fentanyl related deaths have been documented in 1983, 6 in San Diego and one each in Santa Barbara, Santa Clara, Sacramento, San Bernardino, and Stanislaus. The San Diego, Orange, and Monterey County areas account for a significant portion of the deaths.

Alpha-methyl fentanyl was the compound found in nearly all cases analyzed. The drug concentrations found were low but in the general range of concentration found in surgical patients whose breathing must be assisted by a mechanical respirator.

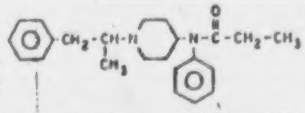
CHEMICAL FORMULAE OF FENTANYL AND ANALOGS



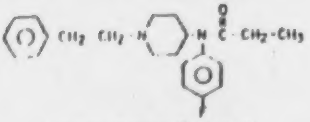
Recently Discovered Unnamed Analog



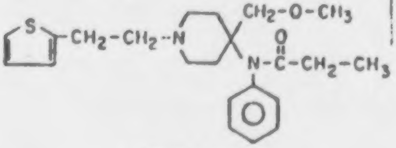
fentanyl (Sublimaze®)



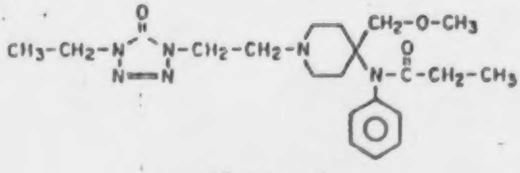
alpha methylfentanyl (China White)



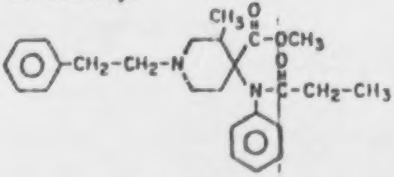
para-fluoro fentanyl



sufentanyl



alfentanyl



lofentanyl

ENFORCEMENT AND DETECTION

Because fentanyl is chemically unrelated to classical narcotic analgesics and is found in such low concentration (trace amounts) in biological fluids and tissues of overdose victims, it is very unlikely that fentanyl compounds will be detected by analytical methods in general use in toxicology laboratories. It is possible that fentanyl and its analogs are in use in states other than California, but this has gone undetected.

Fentanyl compounds are very easily synthesized by a variety of methods. A "Speed" or PCP chemist is capable of performing this synthesis. There are no common precursors to indicate fentanyl manufacturing.

It is not expected that a fentanyl lab would operate for any length of time. One batch would produced enough chemical to last several years.

Fentanyl compounds may be passed off as cocaine and can be snorted. A trace amount in mannitol will produce a "high." The drug is more potent than LSD.

Fentanyl is known to be cut with heroin by addicts who wish entry to methadone programs.

Although most cases of overdose death have occurred in San Diego, fentanyl is known to be available in the San Francisco and Los Angeles areas even though there have been no overdose deaths.

Concerning the future role of the fentanyl analogs as drugs of abuse:

1) This list of fentanyl analogs available on the street will continue to grow and this list will contain at least one compound with a relatively long duration of action.

2) Intranasal administration (snorting) will become a popular (even preferred by some) route of administration.

3) Fentanyl analogs will be used in combination with stimulants such as cocaine.

4) Fentanyl analogs will become popular contraband drugs in prisons, jails and other correctional facilities.

5) The supply of fentanyl analogs will continue to increase, and changes in the supply will be determined by the availability of heroin; i.e., as the overseas supply of opium decreases, the number and availability of fentanyl analogs will increase.

6) The use of fentanyl analogs will spread to other states, including New York, Florida, Texas and Arizona.

What has happened in the last few years is a quantum jump in the state of the art of the illicit drug chemistry. Remarkable sophisticated drugs are not available on the street. For a time, the illicit drug user will be able to use narcotic-like substances that cannot be detected by routine drug abuse analysis. However, as has happened before, quantum jumps in analytical chemistry will be made in the next few years, and the analytical chemist will soon have an assay of analytical techniques with the necessary sensitivity and selectivity.

This article was prepared from information supplied by Dr. G. L. Henderson, Department of Pharmacology, School of Medicine, University of California, Davis, California, 95616. Dr. Henderson has been analyzing blood, tissue, and urine samples for synthetic heroin for the past 3 years. His work was done free of charge, and he received no support from federal or state government. Dr. Henderson will soon cease to conduct research in this area due to "lack of interest." According to Dr. Henderson, the federal government says it is a California problem and the California state government says the problem is too complicated. He also states that apparently all grant money is going towards marijuana and cocaine research, a short-sided policy in light of the rapidly increasing opiate problem and the increased expertise of illicit chemists.

[From Psychiatry Research, 1979]

CHRONIC PARKINSONISM SECONDARY TO INTRAVENOUS INJECTION OF MEPERIDINE ANALOGUES

(By Glenn C. Davis, Adrian C. Williams, Sanford P. Markey, Michael H. Ebert, Eric D. Caine, Cheryl M. Reichert, and Irwin J. Kopin)

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Abstract: Abuse of 4-propyloxy-4-phenyl-N-methylpiperidine, a meperidine congener, produced parkinsonism in a 23-year-old man. Unlike other drug-induced motor disturbances, the syndrome persisted for 18 months and responded to drugs that stimulate dopamine receptors. Biogenic amines and metabolites in the cerebrospinal fluid and microscopic evaluation of the brain at necropsy were consistent with damage to aminergic neurons in the substantia nigra.

Key Words: Parkinsonism, drug-induced, biogenic amines, substantia nigra.

Parkinsonism is a well-recognized common side effect of drugs that either deplete central catecholamines (e.g., reserpine, tetrabenazine) or block dopamine receptors (e.g., phenothiazines, butyrophenones). Drug-induced parkinsonism usually is reversible and abates over several weeks when the offending drug is discontinued.

In this case report, we describe the acute development of parkinsonism in a young man, subsequent to the parenteral abuse of a congener of meperidine. His symptoms persisted for 18 months, although they were controlled successfully with bromocriptine, a potent dopamine receptor agonist.

CASE REPORT

A previously healthy 23-year-old white male was referred to the National Institute of Mental Health (NIMH) for evaluation of a persistent parkinsonian syndrome of 3 months' duration.

He had abused a wide assortment of drugs during the 9 years before his admission. From 1968 to 1976, he had rarely experienced a drug-free interval greater than several weeks. During this period he had experimented with marijuana, amphetamines, barbiturates, and other sedative-hypnotics; he finally chose opiate derivatives (meperidine and codeine) as his preferred drugs. While in college, the patient unsuccessfully attempted to synthesize several opiate derivatives. In the summer of 1976, he attempted and apparently succeeded in the synthesis of 4-propyloxy-4-phenyl-*N*-methylpiperidine, a meperidine congener. This compound was reported by the patient to have produced an opiate-like "high" and other subjective effects similar to those of meperidine. After several months of intravenous and intramuscular self-administration of the home-synthesized compound, the patient prepared additional batches, but took synthetic shortcuts. In November 1976, after several days of injecting this "sloppy batch," he developed a state of muteness, severe rigidity, weakness, tremor, flat facial expression, and altered sensorium. He was admitted to the psychiatric ward of a general hospital with an initial diagnosis of catatonic schizophrenia. On examination he was gaunt, lying motionless in bed unable to speak. He was unresponsive to most verbal stimuli, but responded slowly to simple instructions. His upper extremities showed waxy flexibility and lead-pipe rigidity. Thick saliva had accumulated in his mouth. The remainder of the physical examination was negative, and routine laboratory tests were normal. A short course of haloperidol failed to bring about improvement although electroconvulsive therapy did result in reduced motor retardation. After consultation with a neurologist, the patient was treated with levodopa/carbidopa, benztropine, and diazepam. He improved markedly.

In February 1977, the patient was referred to NIMH for further investigation of his parkinsonism. At that time he was taking levodopa/carbidopa (25 mg and 250 mg) six times a day and benztropine, 0.5 mg t.i.d. He complained of slowed thoughts. Mild blepharospasm and bradykinesia were the only neurological signs noted. There were no abnormalities of speech, hallucinations, delusions, ideas of reference, or other evidence of a thought disorder. His mood was depressed, and his affect was flat. Although complaining of slowed thoughts, the patient showed few signs of intellectual impairment. Cognitive evaluation revealed no abnormalities suggestive of focal impairment. His scores on the Wechsler Adult Intelligence Scale were 109 on the verbal scale and 100 on performance scale. Significantly, he was most deficient on those subtests that were timed (e.g. arithmetic. block desgin), with a "loss" of 21 points from his performance score due to slow execution. The patient could perform consistently well on serial learning memory tests, which are impaired in most individuals with idiopathic parkinsonism (Caine et al., 1977). Neither he nor his family recalled a gradual development of symptoms, and handwriting samples from the year preceding his sudden deterioration showed no change.

The patient had no family history of neurological disease. Routine laboratory tests were normal. Serum copper, ceruloplasmin, slit lamp examination, cerebrospinal fluid (CSF) protein, glucose, immunoglobulins and cell count, electroencephalogram, skull films, brain scan, and computerized tomography (CT scan) of the head were also normal.

When therapeutic agents were discontinued, severe bradykinesia, generalized rigidity, and a mild tremor progressively developed over a 3-day period. Speech and swallowing were severely impaired and urinary retention developed. There were no pyramidal or cerebellar signs. Resumption of treatment with levodopa/carbidopa (Sinemet) brought about rapid improvement. Bromocriptine (100 mg/day) was equally effective and was continued as the drug of choice because of its longer duration of action and because the patient tended to abuse levodopa.

After maintenance on bromocriptine for 6 months, the patient was readmitted. His medication was discontinued for 3 days, whereupon his symptoms reappeared but were milder than during the previous admission. At this point his CSF levels of homovanillic acid (HVA), 5-hydroxyindoleacetic acid (5HIAA), and norepinephrine (NE) were all well below values seen in 15 patients with idiopathic Parkinson's disease and 25 normal controls (Table 1).

TABLE 1.—BIOGENIC AMINES IN THE CEREBROSPINAL FLUID OF THE PATIENT AND CONTROLS

	Patient	Parkinson's disease (*n*=15)	Normal (*n*=25)
HVA (ng/ml±SD)	5.0	17.5±11.6	43.0±32.5
5HIAA (ng/ml±SD)	5.0	13.7±11.6	18.3±10.0
NE (pg/ml±SD)	105.0	215.0±135.0	374.0±180.0

Fifteen months after the onset of illness, the patient required only 20 mg/day of bromocriptine but continued to have mild bradykinesia which became more prominent when the dose was reduced further. At 18 months, bromocriptine was discontinued; the patient exhibited no extrapyramidal signs but still complained of slowed thoughts.

The patient continued to abuse many drugs including cocaine, codeine, dihydromorphinone and $_{L}$-dopa, and in September 1978 he was found dead of an overdose. A blood level of 0.23 mg/l of cocaine and <0.05 mg/l of codeine was found on autopsy.

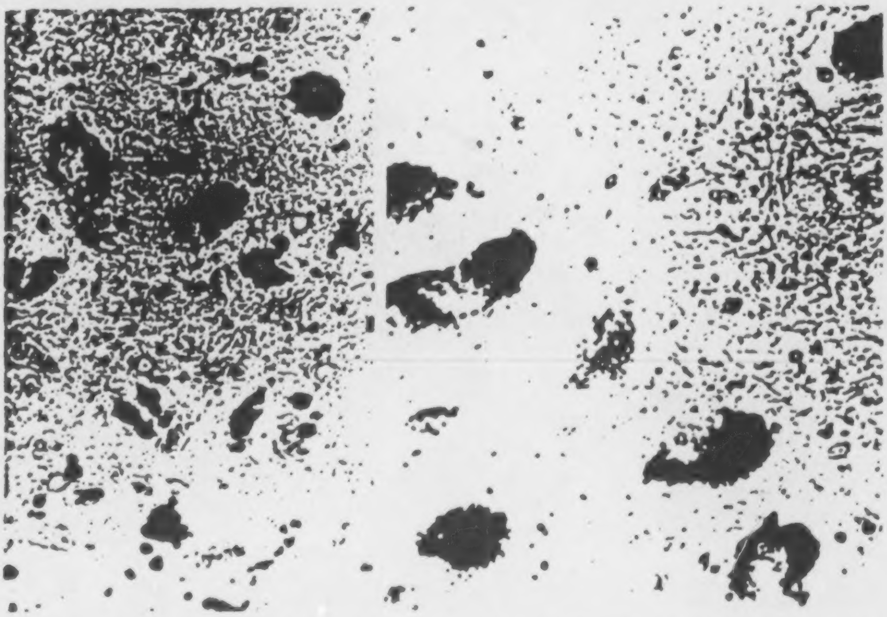
On gross examination of the brain, irregular patches of tan discoloration were seen within the ventricular lining, and microscopic examintion disclosed destruction within the substantia nigra (Fig. 1). Much of the neuromelanin pigment was extracellular and within microglial cells. A rounded eosinophilic intracytoplasmic "Lewy" body, characteristic of Parkinson's disease, was noted (Fig. 2). The pigmented cells of the locus ceruleus were intact. The ependymal lining was focally disrupted by numerours partially fibrotic plaques, suggestive of a prior ependymitis. Other autopsy findings included; pulmonary vascular crystalline material, pulmonary microgranulomata, pulmonary and hepatic intracellular crystalline matieral, hepatic triaditis, and the presence of scars at injection sites on the arms.

COMPOUND IDENTIFICATION AND SYNTHESIS

The patient chose to synthesize 4-propyloxy-4-phenly-*N*-methylpiperidine (PPMP) because it was known to be a more potent analgesic than pethidine (Janssen and Eddy, 1960) and could be readily produced from the commercially available, unrestricted chemical 1-methyl-4-piperidine (MP) (Berger et al., 1947; Ziering et al., 1974).

Over a period of 5 to 6 months, the patient repeated the synthesis (Fig. 3) but with reduced reaction times and higher reaction temperatures; finally he neglected to isolate and crystallize the product properly. Duplication of the patient's reaction conditions, however, yielded relatively pure 4-hydroxy-4-pheny-*N*-methyl piperidine (HPMP) (Fig. 3), identical to traces of material found on the patient's laboratory glassware.

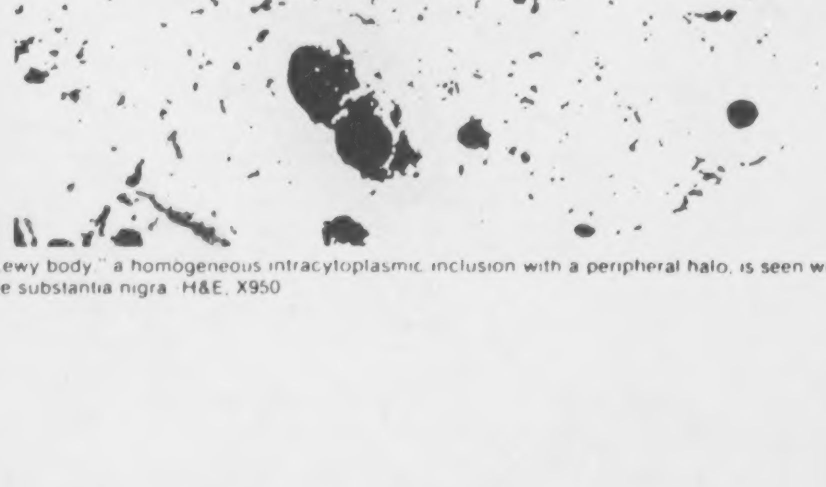
Fig. 1. Photomicrographs of the substantia nigra and locus ceruleus



Left: Destruction within the substantia nigra. Note the incontinent and phagocytized neuromelanin pigment (melanin stain, X400).

Right: A photomicrograph exhibiting the intact pigmented neurons of the locus ceruleus is provided for comparison (melanin stain, X400).

Fig. 2. Lewy body



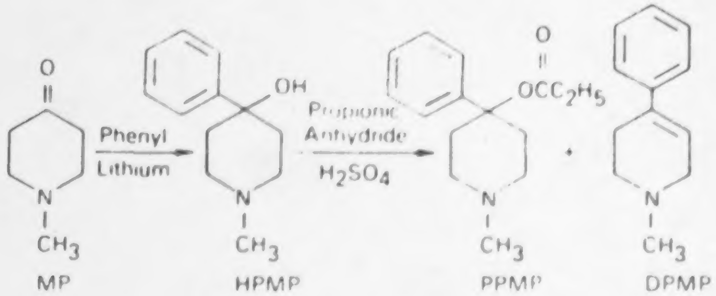
"Lewy body," a homogeneous intracytoplasmic inclusion with a peripheral halo, is seen within the substantia nigra (H&E, X950).

Prelimianry testing of PPMP in rats has confirmed a short-acting analgesic activity with the development of rapid tolerance. When treated with one milligram (3 mg/kg), rats developed a catatonic state with rigidity lasting about ½ hour, suggesting greater potency for catatonia than morphine.

DISCUSSION

The development of a persistent parkinsonism in our patient was probably due to this "sloppy batch" of PPMP. The compounds injected appear to have been a mixture of the compounds HPMP, PPMP, and dehydro-4-phenyl-*N*-methylpiperidine (DPMP) (Fig. 3). The diagnosis of idiopathic Parkinson's disease or other causes of parkinsonism seem unlikely because of his youth, the acute onset, the chronic course with return to normal function after 18 months, the necropsy evidence of structural damage to the substantia nigra, and the temporal relationship to the self-administration of these compounds.

Fig. 3. Reaction scheme



Synthesis of patient's target compound 4-propyloxy-4-phenyl-*N*-methylpiperidine

The CSF values of HVA, 5HIAA, and NE were far below normal and below those found in most patients with Parkinson's disease. Although our patient's bromocriptine had been discontinued only 3 days before his lumbar puncture, we feel that it is unlikely that the drug's pharmacological effecs accounted for the striking reduction of the CSF dopamine and serotonin metabolites and NE since the levels of these compounds were below those found in Parkinson's disease patients treated with similar doses of bromocriptine. In our experience with idiopathic Parkinson's disease, bromocriptine reduces HVA and NE by one 50% and does not alter 5HIAA. These values suggest severe damage to dopaminergic neurons and prominent alteration in noradrenergic and serotoninergic systems as well. Furthermore, the clinical response of this patient to dopamine receptor stimulators and a normal caudate at necropsy suggest that the postsynaptic neurons remained functionally intact. This mechanism for the development of a parkonsonian syndrome contrasts with that responsible for the parkinsonism resulting from dopamine receptor blocking actions of butyrophenones and phenothiazines.

In summary, this appears to be a case of drug-induced parkinsonism with specific structural damage to the substantia nigra. Unlike other drug-induced motor disturbances, the syndrome persisted for 18 months and responded well to drugs which stimulate dopamine receptors. The levels of biogenic amines, and metabolites in the CSF, the clinical symptomatology, the therapeutic response to dopamine receptor stimulation, and the microscopic evaluation of the brain at necropsy are all consistent with drug-induced damage to aminergic neurons in the substantia nigra which resulted in a parkinsonian syndrome.

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[From the Jacksonville (FL) Times/Union, July 14, 1985]

CONGRESS SHOULD ACT QUICKLY TO END FLOW OF "DESIGNER DRUGS"

The relatively quick response by the Justice Department to write proposed new legislation to slam the door on a new scheme in the manufacture of dangerous drugs deserves equally quick enactment by the Congress.

The latest subterfuge used to make profits from the sowing of death and human degradation through the sale of drugs for "recreational" use has been identified as the "designer drug" racket.

Present law defines the chemical makeup of heroin and cocaine by their molecular structures and, fiendishly, some amoral people have been concocting drugs with slightly different molecular structures that have the same or even more deleterious effects on the human system as do heroin and cocaine.

When one looks at the record of death and destruction from drug abuse by pathetic addicts, one cannot but be appalled that individuals would manufacture new chemicals designed to perpetuate the horrors of drug abuse and pretend that they were within the law—within their rights to peddle a new source of death and human devastation.

In May, during hearings of the Senate Appropriations Committee, of which he is a ranking minority member, Sen. Lawton Chiles, D-Fla., confronted Attorney General Edwin Meese with the problem of "designer drugs" and how criminally intended manufacturers were evading the purpose of the law with the manufacture and sale of these new drug products.

Meese's Justice Department was quick to respond and filed a bill that would change the law so that manufacture and use of potentially destructive drugs would send such people to jail for up to 15 years and impose fines up to $250,000.

With more than 1,000 deaths a year each year over recent years from abuse of heroin and cocaine, the American people do not need a new killer loose among them, one that poses as perfectly legal—if absolutely immoral.

Meese has stated in connection with other drug-abuse cases that "people have to learn that there is no such thing as a harmless recreational drug," adding that by participating in the illegal activities they are supporting the killers of thousands of addicts, the murderers of law enforcement officers and the ruination of the lives of thousands more.

The greater tragedy of drug abuse is that it is gaining younger and younger populations continually.

Congress now must move quickly to shut the door on "designer drugs."

[From the San Francisco Examiner, Aug. 29, 1984]

DEADLY NEW DRUG HITS STREETS HERE

(By Seth Rosenfeld)

REDWOOD CITY.—When police found Anthony Gilbert Flores behind a Menlo Park Hamburger joint just before midnight June 30, rigor mortis had already set in. The 36-year-old self-employed carpenter was still standing beside the open driver's door of his Chevy truck, leaning over the seat. The needle was still in his arm.

Instead of heroin, police suspect, Flores got fentanyl, a powerful synthetic narcotic up to 7,000 times as potent as an equal weight of morphine. The drug has popped up with increasing frequency in the Bay Area and has left a wake of overdoses and frustrated narcotics officers.

"This is causing deaths," said Menlo Park detective Mark Kinsey. "It's coming around more and more. We're having lots of talk about OD's. The word's getting around that there's some bad stuff out there."

"Yes, there's been an increase in overdoses." said San Mateo County Sheriff's detective Terry Mackey. "This stuff is on the street. It's extremely dangerous."

At least 47 people have died of overdoses of the deadly heroin look-alike since 1980, when it was first reported in Southern California surburbs, according to Dr.

Gary Henderson, an associate professor of pharmacology at the University of California at Davis. Henderson is studying the drug under a contract with a state alcohol and drug program department. Forty-four of the deaths have been in California, one in Arizona and to in Oregon.

In the Bay Area, police during the last six months have encountered the drug on city streets for the first time. Within the last two months, at least six people in Northern California have died from it, according to Henderson. He said he expects pending test results to bring the figure to 12.

"It's all over the place in the Bay Area," said Henderson, who has analyzed the drug for police departments. "The overdose cases we get are the bare tip of the iceberg."

In its pharmaceutical form, tradenamed Sublimaze, fentanyl was first developed in the late 1950s as a general anesthetic, he said. Although the chemical structure of fentanyl is unrelated to that of organic opiates, it has the same effect, blocking out pain and depressing the respiratory system. Pharmaceutical fentanyl is about 80 times the strength of morphine and is now used in 70 percent of all major surgeries, usually with respiratory assistance equipment, Henderson said.

Illicit forms of fentanyl began to appear on the streets of Southern California about four years ago. Since it averaged about 100 to 200 times the power of morphine, it was heavily diluted with milk sugar and sold as "China white," or "Persian white," the highest quality heroin available, Henderson said. The mixture was sometimes heated and caramelized and sold as lumps of "Mexican brown" heroin, too.

Until recently, fentanyl was found primarily in Southern California and the South Bay Area, although it cropped up briefly in Oakland an East Palo Alto last year. Recently, it's appeared in San Francisco, Marin, San Mateo and Monterey counties, while coming back strong in Alameda County and in northern Santa Clara County, according to Henderson and the police.

Marin County Sheriff's detective Jerry Mattos said an undercover agent recently purchased one-tenth of a gram of the white powder in a paper bundle for $110. "It's the first time we found it on the street to buy," he said.

Users can't tell the difference between fentanyl and heroin, which is usually injected or snorted, Henderson said. But since fentanyl is so much stronger, the slightest miscalculations in dosage by dealers and addicts have caused overdoses and death.

"Its action is almost instantaneous. We've had people die literally with the needle still in their hand." said Mackey of the San Mateo County sheriff's office. "It's very difficult to control its dosage."

The biggest cluster of recent fentanyl deaths has occurred in the South Bay, according to Henderson.

The San Mateo County coroner's office has postively identified fentanyl as the cause of to recent Peninsula deaths, one of them a 36-year-old Vietnam veteran. Menlo Park police suspect it caused two others earlier this month.

The new street drug, which authorities believe is being manufactured in clandistine labs in Southern California, in some ways has stymied law enforcement. It is so powerful that most local police and coroner's laboratories lack the high-tech equipment to test for it.

Sgt. Dennis Downum of Oakland's vice squad said that such tiny amounts of the drug produce fatalities that "a lot of times in an autopsy they can't find it" and have to send body fluid samples to state and federal labs.

"It's really putting handcuffs on us because we can't test it," said Mackey. "We need some legislative changes."

But as lawmakers have expanded statutes in an effort to lengthen the arm of the law, illegal fentanyl manufacturers and dealers have tried to stay just beyond reach by slightly altering the drug's chemical composition to produce a new version, or "analog," not covered under state and federal statutes—a tactic used with other illicit drugs.

Last week, federal drug laws were amended to include a pharmaceutical analog of fentanyl called "alfentanyl." And state legislation to bring California's drug laws in line with federal laws introduced by Assemblyman William Filante, R-Greenbrae. Filante sponsored the bill after reports that two youths from his district died of fentanyl overdoses, said Filante aide Sue Doyle.

"They're having a terrible time with fentanyl," Doly said. "Kids think it's the same strength as heroin and its a lot stronger. They're just killing themselves with it."

But despite the state and federal efforts, several forms of fentanyl are not yet covered by the laws, according to Henderson. These include the newest and most deadly form of fentanyl to date, 3-methyl-fentanyl, which is up to 7,000 times the strength of morphine, Henderson said.

"It's one of the most powerful substances known," Henderson said. "You could use a syringe, wash it out, and still you'd get an effect from just a few molecules."

Henderson believes this most lethal form of fentanyl is responsible for recent deaths in the Bay Area. He estimates that about 20 percent of what is sold on the streets as heroin is actually a form of fentanyl.

[From the Ann Arbor (MI) News, May 12, 1985]

DESIGNER DRUGS

(By David M. Dworkin)

It can be 8,000 times stronger than pure heroin. It costs less than $1,000 to make $5 million worth at bargain street prices. When properly diluted, it gives the user the exact same high as top grade heroin.

And, until late last month, it was totally legal.

The federal government's Drug Enforcement Administration calls it 3-Methyl Fentanyl (3MF), and in the shooting galleries of California it is occasionally passed off as China White, a particularly pure grade of heroin.

But this isn't heroin, and that's what has the drug enforcement community worried.

The substance finally identified as 3MF was created by a kitchen chemist in a clandestine laboratory. And by the time it was declared illegal on April 25, the chemist who made it had stopped production to work on a new test tube version of herion, officials believe. Almost identical to 3MF, it too will be totally legal until it is discovered, analyzed and listed as a controlled substance by the DEA. That could take a year or longer. And then the process will begin again, with the chemist designing a new drug that is just as potent, just as dangerous—and legal.

Welcome to the age of "designer drugs."

Designer drugs are the latest technological counteroffensive against the government's war on drugs. Although confined to the West Coast for now and possibly the product of a single chemist, test-tube drugs are becoming increasingly prevalent. More than 20 percent of California's heroin supply may be made in one clandestine laboratory, officials suspect.

And at least 90 of its users have become its victims—killed by massive overdoses of badly "cut," or diluted, batches.

"It's scary," says Robert J. Roberton, the director of California's Division of Drug Problems. "I estimate this stuff could replace heroin."

So potent are these designer drugs, most experts agree that with proper distribution one chemist could supply the nation's entire heroin supply indefinitely.

Kitchen chemistry labs in the United States could replace the poppy fields of Asia and Mexico. The government's anti-drug war—based on armies of customs agents guarding borders and airports—could be rendered obsolete.

And that's not a situation that organized crime, now reaping billions in profit from traditional poppy-grown heroin, is likely to accept without a fight.

Roberton predicts large-scale wars between gangs carving up distribution territories for the new narcotics. The prize for victory, says Roberton, is 10 times current profits and virtual immunity from successful prosecution.

Organized crime, says Roberton, has hesitated to get on the designer drug bandwagon so far. But if one chemist can supply 20,000 junkies, a more involved effort could gut nationwide heroin prices, currently inflated by the drug's relative scarcity.

This gives the mob an even greater interest in finding out who the mystery chemist is. "It would be safer for him." says Roberton, "if he were caught by the feds."

"All the signs indicate that designer drugs will be a major part of the drug abuse problem of the future," says Sen. Lawton Chiles (R-Fla.), who has introduced new legislation on the problem. "If that proves to be the case, the public health consequences of drug use may be entering an entirely new and frightening dimension."

According to a recent study done by the National Institute on Drug Abuse, illegal drug use is already a staggering national problem, costing the United States $46.9 billion dollars in 1980 in crime, enforcement costs and prevention, not to mention additional billions in lost tax revenues.

What exactly are designer drugs and why do they pose such a serious threat to the fight against drug abuse?

The answer to that question goes back to 1969, when Congress passed the Controlled Substances Act. Under the Act, drugs are "scheduled," or identified as illegal, by their molecular structure.

This was done to counter the early test tube drugs such as LSD, PCP and variations of amphetamines.

Later, in 1979, underground chemists began experimenting with the molecular structure of a commonly used anaesthetic that was similar to heroin. The drug, called fentanyl, was slightly altered, massively increasing its potency and rendering it legal because its chemical structure was no longer "scheduled."

Now, every time the federal government discovers a fentanyl designer drug, or analog, and makes it illegal, the chemist only has to add one extra molecule of carbon to get around the law. The new fentanyl analog is just the same as the old one with one exception: It is legal.

Although recent improvements in the Controlled Substances Act have made it easier to schedule new analogs, a chemist with a subscription of the Federal Register can easily stay ahead of the DEA.

According to Gary Henderson, a pharmacologist at the University of California at Davis, there are tens of thousands of possible chemical analogs. Every time a new one is scheduled, it can easily be discarded.

Torrey Johnson of the California Department of Justice's Crime Lab, is worried that chemists who continue to alter the analogs every time they are scheduled will turn this trend "into a horror story." "We don't want to get into a paper chase with these people," he says.

According to Peter Evans, deputy district attorney for Marin County, Calif., broader scheduling laws must be enacted if the problem is to be contained.

"People have been arrested and they've had chunks of this stuff and you couldn't do anything about them," adds Roberton. "In fact, you had to return their materials to them."

Evans acknowledges he has had to let "somewhat less than half a dozen" dealers go when their fentanyl was found to be unscheduled, but he says that no one has ever requested their drugs back.

"I think they know a good thing when they see it," he says. "Several more cases are pending lab test results, which can take months to complete."

Addicts are becoming aware that the new analogs are stronger and less adulterated than typical street heroin, making them increasingly popular.

The high concentrations of the drugs are causing even more problems in treatment. Many addicts are now going to drug treatment centers with track marks on their arms and symptoms of severe heroin withdrawal, but with no traces of narcotics in their blood or urine.

Only two labs in California have the ability to find the minute amount of fentanyl present in the specimens. By the time results come back positive, allowing the center to administer methadone, the addict has already suffered through the worst of his withdrawal or quit the program.

Roberton has made designer drugs a high priority of his department and has become the leading national authority on the subject, testifying at federal hearings and producing educational videos on the new drugs.

There are currently 10 different known analogs on the streets of California, according to Roberton, three of which have been scheduled and are now illegal.

At least one batch is responsible for the death of 90 people. In its pure form it was more than 8,000 times the strength of heroin. "You can put enough on a postage stamp to kill probably a couple hundred people," says Roberton. "You're talking about millionths of a gram."

Actually, Roberton is quite impressed with the overall quality of the analogs he sees coming off the street. "It's got to be cut absolutely to perfection," he says. "Whoever's cutting it is doing a fantastic job in quality control. The guy must be brilliant because (otherwise) he would have all the addicts dead in a week."

Most recent fatalities, says Roberton, represent "the novice coming in or the addict who's been off the street for a few months," rather than steady users. There is also a new user of heroin according to Roberton: "the heavy cocaine user who wants to come down . . . We think they're unsophisticated enough to overdose on it."

A high degree of expertise is needed to work with designer drugs. While not difficult to make, they are extremely dangerous to handle and to dilute. Simply inhaling the air near a batch of 3MF or touching it can cause immediate death. "If you're not careful—gowned up, with a proper mask and gloves on—you're going to die," Roberton said.

David Hoover of the DEA claims this kind of danger is the chief and perhaps only limiting factor on the future growth of designer drugs. But Roberton is not so confident that fear will overcome greed among chemists. "There are always chemists out there prepared to make a fast buck," he says.

In their haste to get in on the designer drug bandwagon, other kitchen chemists have experimented with making analogs of everything from cocaine to Quaaludes. One defective batch of analog Demerol has left more than 300 people with irreversible brain damage.

According to Roberton, a careless chemist may have heated an ingredient too long, thereby changing its form. When addicts take the drug, called MPTP, "it goes straight to the brain . . . and destroys the same cells that are destroyed in Parkinson's disease." (See related story on this page.)

Although it is not yet confirmed, California drug enforcement officers believe another batch of poisonous MPTP is on the streets.

"What do they care," said Roberton of the people who push these drugs. "There's no animal trial. It goes from the lab to the street, and the first animal it sees is a human. Nobody sends flowers when an addict dies."

"When this rally catches on," he said of the analogs, "you'll have chemists making all kinds of garbage all over the country."

In March, Sen. Chiles introduced legislation calling for a Congressional study of the designer drugs problem, including:

A comprehensive assessment of the current and potential problem;

A study of proposals for new enforcement strategies; and

Recomendations to Congress for necessary legislation.

While Roberton acknowledges enforcement must be persistant he firmly believes prevention is the only strategy that can make a serious dent.

"Clearly, heroin has been outlawed since 1914 and it hasn't made any difference," he says. "I'm convinced after 30 years in the drug biz, that it has got to be prevention. This state is pouring millions into prevention, working with families to strengthen families. We now do prevention down to 5½-year-olds."

Whereas the past approach was showing scare films about drug abuse to junior high and high school students, Roberton says the new approach must be towards strengthening the family. "Now we are talking to children about their feelings, how they feel about their mum and their dad, their brothers, whatever. And they don't talk about drugs necessarily, but they do talk about the problems that lead to drug addiction."

Roberton is not optimistic about the future.

"We are caught in a technological terror now because we have the sophistication," he says. "I think we're getting to the end of the '80s and the beginning of the '90s, where people are going to ask for the mood that they want. They're are going to say, 'Look, I don't want a hangover and I want it to last an hour because I've got to go back to work.'

"Unfortunately with the technology and the expertise we have, I think we're working towards that. This analog game is going to make it increasingly difficult for the drug enforcement field."

life

DESIGNER DRUGS ACT LIKE HEROIN, BUT CAN BE LEGAL

(By Audrie Krause)

To a user, fentanyl and its derivatives look and act exactly like heroin.

But chemically, the so-called "designer drugs" are nothing like the substance they are being substituted for. And in some cases, the substitutes are not illegal.

"Designer drugs" is a term first used by Dr. Gary Henderson, an associate professor of pharmacology at the University of California at Davis.

Henderson has been studying the heroin substitutes since they first showed up in California in 1979.

He said the term, "designer drugs," occurred to him when he saw a sample of fentanyl that had been cut with heroin.

" It gives you everything you want. It's more potent than heroin, it has the same effect, it's legal, it can be formulated for shooting, snorting or smoking," he said. "What they're doing is designing the drug to any need."

Chemists have also manufactured a synthetic version of Demerol that has been sold in the Monterey Bay and San Jose areas as "new heroin," but the product was apparently contaminated with a substance that caused users to develop Parkinson's disease.

"That had hideous results, and those people are affected for life," said Janet Bair, division manager of Fresno County's substance abuse program.

So far, officials at several Fresno drug treatment centers say, they have seen very few clients who have used the "designer drugs."

"I don't think that, locally, we're having much of a problem with it," said Robert W. Klise, executive director of The Third Floor, a residential drug treatment center.

"Most people don't really tell us," said Dolores Senna, a mental health nurse with the Olive Street Bridge, an outpatient treatment center.

Henderson said the fentanyl derivative that is being sold on the street now is a thousand times more potent than heroin.

"The actual amount you inject, or snort, or smoke would be about what you could see with the naked eye," he said.

Like heroin, the substance is cut with lactose, or milk sugar. Because the drug is so potent, he said, the average dose used by an addict is about 99.9 percent lactose.

Synthetic heroin differs from the real thing in more than one way. Methadone, Demerol and Darvon are also synthetic narcotics, but they are chemically similar to morphine and codeine, the two opium alkaloids derived directly from poppies.

Heroin itself is a semi-synthetic derivative of morphine and is very similar to it chemically.

But fentanyl is an entirely different substance, chemically, although it produces the same euphoric high as other narcotics. And, like heroin, it is addictive.

Fentanyl derivatives are compounds that are chemically similar to fentanyl but have slightly altered molecular structures.

Narcotics officials have identified at least five derivatives of fentanyl that are being or have been sold on the street as heroin.

Fentanyl itself is a commonly used anesthetic, although it's use is restricted. Henderson estimates that it is used in about 70 to 80 percent of all surgeries.

Fentanyl and its derivatives are generally sold on the street as "China White."

At present, only two of the derivatives—alpha methyl fentanyl and sufentanyl (which is also used as an anesthetic)—are classified as illegal drugs.

The other three are technically legal.

That is because drugs must be specifically classified as illegal, and the classficiation can be made only after the drugs are thoroughly tested.

Even when a drug is classified as illegal, chemists can make slight modifications in the molecular structure and produce a derivative that is legal. That is what chemists have been doing with the fentanyl derivatives.

Henderson said fentanyl has turned up in almost every county in the state, except for the most northern ones.

But all reports of overdoses have come from suburban and rural areas, rather than major cities.

Officials do not know how widespread the use of fentanyl is, although Henderson is doing some studies in an effort to find out.

Bair said reports suggest the contaminated drug is moving south from the Monterey Bay area.

Although 77 deaths from overdoses of synthetic heroin have been reported in California in the past four years—including at least two in Fresno County—narcotics officers and substance abuse workers are only now beginning to learn much about fentanyls.

Officials from the state Department of Alcohol and Drug Abuse will be in Fresno on Friday to brief local drug abuse workers on the subject.

[From the Wall Street Journal, Mar. 8, 1985]

DESIGNER DRUGS: AN ENFORCEMENT NIGHTMARE

(By Jack Shafer)

Heroin's surreptitious journey to America has traditionally begun in foreign lands where its raw ingredient Papaver somniferum, opium-poppy, is cultivated. But in 1979, underground chemists in California cracked the foreign connection with "designer drugs," synthetic drugs made in clandestine laboratories for pennies a dose. While not the last shot to be fired in the war on drugs, the designer drugs may be the decisive one. The government has yet to find a way to stamp them out.

These high-tech highs were designed to look like heroin, pack its euphoric punch and stave off withdrawal. But they had another designer wrinkle. By subtly modifying the molecular structure of fentanyl, a commercial synthetic opiate, the chemists created analogs or chemical cousins of fentanyl that were not prohibited by the drug law. These drugs were completely legal to make and use.

Consider the enforcement dilemmas the designer drugs present:

Their formulas can be found in almost any university chemistry library;

They can be made in undetectable bathroom-size labs, beyond the reach of customs officers and eradication teams;

From $500 worth of chemicals one can make $2 million worth of "synthetic heroin";

One lab can meet the world's demand for heroinlike drugs without harvesting a single opium-poppy;

Because fewer people need to be cut in on the action the profit margin is higher;

As fast as the government outlaws designer drugs the chemists can synthesize new ones.

Actually, the chemists have been spinning off analogs faster than the government has outlawed them—so far, only one of a half-dozen fentanyls has been banned. They are now so ubiquitous in Calfornia that Robert J. Roberton of the state's Division of Drug Programs estimates that up to 20% of California's 100,000 heroin users are now taking one of them. The fentanyl analogs have killed more than 85 people so far, and continue to add to the body count at the rate of two a month.

How many fentanyl analogs are possible? Gary Henderson, a pharmacologist at the University of California estimates their number in the tens of thousands. But other synthetics can be re-tailored into legal heroin substitutes, too. In the summer of 1982 an analog of meperidine (the painkiller marketed as Demerol) made the rounds in San Jose, Calif.; an impurity in the concoction gave seven heroin users irreversible brain damage. The drug vanished from the market when the medical warning went out, but we haven't seen the last of this analog. In recent years, independent chemists in Vancouver, British Columbia, and Bethesda, Md., have gone directly to the chemical literature to find the formula for the drug and then poisoned themselves with it. For those who are too lazy to look up the original formula, a simplified 16-step, photocopied recipe for it is now circulating in California drug circles.

The designer market, however, is not limited to heroin substitutes. Nature has provided the chemical patterns for millions of legal drugs of abuse. Nearly every drug, from cocaine to marijuana, LSD to Quaalude (methaqualone) can be mimicked by cheap designer drugs. In fact, a steady stream of designer drugs based on illegal synthetics such as PCP (piperidine), Quaalude, methamphetamine (P2P) and the psychedelics have appeared on the market over the years. If chemists ever dedicate themselves to churning out analogs, the government will find itself playing a permanent game of catch-up. "Eventually the list of illegal drugs is going to be as long as the New York telephone book," said Mr. Henderson.

The federal government is attacking designer drugs with new regulatory powers it won in the crime bill passed by Congress last October. The months—or years—process of banning designer drugs had been shortened so that all the governments had to do is identify the new drug, publish its formula in the Federal Register and, *voila*, 30 days later it is as illegal as heroin. But even if the government found a way to ban millions of designer drugs before the fact, clandestine labs would continue to be an unstoppable source of synthetic drugs. The laws already on the books have failed to put so much as a dent in the supply of illicit synthetics. Police close more than 200 clandestine labs annually, but according to the National Narcotics Intelligence Consumers Committee, a federal task force, another 800 labs go undetected each year. Because a single lab can put millions of doses on the market, hundreds of millions of doses of the synthetics still find their way to the market each year.

Synthetic drug profits are so astronomical that many chemists are more than willing to risk up to 40 years in prison and $500,000 in fines. Similarly, chemists have shrugged off recent laws that control the raw ingredients needed to make PCP and methamphetamine by switching to other precursor chemicals or buying what they need on the black market. If the government licensed all lab equipment and chemicals, chemists still would be able to synthesize drugs from earth, air, fire and water using pressure cookers, hot plates and garden hoses.

Since passage of the prohibitionist Harrison Act of 1914, America has been the prime mover in the international system of drug control. by attacking the supply of illicit drugs at their foreign sources, the international system has sought to reduce the supply and price drugs out of the reach of users and potential users.

But controlling the supply is no longer a simple matter of sealing the border drug-tight and uprooting every coca, opium-poppy and marijuana plant on earth. Designer drugs, whether they are banned or not, are impervious to international treaties, eradication schemes and border seizure. Already the fentanyl analogs have spread from their California proving grounds to Arizona, Oregon and New York. As the designer drugs proliferate—and there is no reason to believe they won't—they may well topple the international system of drug control and render the war on drugs permanently unwinnable. There will be just too many inexpensive drugs and too many enterprising druggists to stop.

The drug war will continue with shots being exchanged on both sides. But for now the government is on the run.

[From the Corpus Christi (TX) Caller Times, May 26, 1985]

DESIGNER DRUGS—A NEW BREED OF RENEGADE CHEMISTS ARE CREATING NEW DRUGS AND NEW HEADACHES FOR LAWMAKERS

(By Jeff Leen)

The drug, 1,000 times more powerful than heroin, is designed in a clandestine lab by a renegade chemist, a brilliant phantom who has earned the grudging respect of law enforcement pharmacologists.

It is cut innumerable times and passed off as Persian White, the caviar of heroin. It is sold in the redwood suburbs north of San Francisco to chic young professionals, junkies in hot tubs.

It killed 49 people last year. It is cheap, addictive and perfectly legal.

By tinkering with the molecular structure of fentanyl, a synthetic painkiller routinely used in surgery, the unknown chemist has created the latest fad to come out of California—"designer" heroin.

"We're talking about a world-class medicinal chemist," said Dr. Gary Henderson, a pharmacologist at the University of California at Davis who coined the term "designer drugs" for the synthetic substances that began cropping up on the West Coast in the late '70s.

"First they said it was California craziness, 'It's going to go away.' I don't see it. Something that's 1,000 times more powerful than heroin, dirt cheap to make, hard to detect, you can smoke it, snort it, you don't have to inject it . . . ."

The state-of-the-art drug poses unique problems. Coroners cannot detect it in overdose victims. And there is a laboratory loophole that could endlessly frustrate the law: New variations can be turned out faster than they can be identified and outlawed. And when they are finally made illegal, a sophisticated "designer" can create a new, legal drug merely by altering the molecule. The users are the guinea pigs.

"This is very, very frightening," said Chauncey Veatch, director of the California Department of Alcohol and Drug Programs, which expects 78 people to die this year from designer drug overdoses.

To date, 90 people have died from such overdoses, 13 in the first four months of this year. The fear is that the new heroin will sweep the country. Three designer drug deaths have occurred outside California, two in Oregon and one in Arizona.

"As California goes, so goes the rest of the nation. That's what happened with LSD," warned Frank Chellino, U.S. Drug Enforcement Administration spokesman in Miami.

In March, U.S. Sen. Lawton Chiles, D-Fla., proposed legislation that would focus federal attention on the problem. His legislation is currently pending before the Senate Judiciary Committee.

"This will come out of California and, look out, it'll come across fast," Chiles said. "It's so easy to produce these drugs in small labs: A $500 investment in chemicals can produce a $2 million batch of synthetic heroin. There's just too much money there. It's just got to spread."

Henderson said he has heard that underground chemists are coming to California to learn how to make fentanyl.

Right now, law enforcement can do little. If DEA agents raided a designer drug lab tomorrow, chances are they couldn't make any arrests.

"I think (arrests would be) very doubtful," said Gene R. Haislip, director of the DEA's office of diversion control.

It used to take months, even years, to list a drug—by chemical formula—in the Controlled Substances Act. "We can't take action based on a suspicion. We have to have data," Haislip said. Now, under legislation passed last year, a drug can be made illegal in 30 days.

"We're hoping this new authority will enable us to nip this in the bud and keep this from spreading," Haislip said. "But I can't say that it will."

Thirty days is still plenty of time for a smart designer to change the formula.

So far, DEA chemists have uncovered 10 varieties of fentanyl. Only two are illegal, and two more are scheduled to be outlawed soon. The newest and deadliest, 3-methyl-fentanyl, became illegal April 28.

"We believe it is the one connected with the deaths in California," Haislip said.

Once 3-methyl-fentanyl is outlawed, there are plenty of others waiting in the lab. Chemists have created 200 more variations of fentanyl in industrial laboratories. The variations could go as high as 1,000.

"If you have yourself boxed in where you have to have the formula, it looks like those fellows can always stay ahead of you," Chiles said. "They're going to have to change the definition of the crime."

Chiles' proposal would direct the government to include designer drugs in a strategy plan scheduled for release in July. The senator also wants the congressional Office of Technology Assessment to study the drugs and find out what the government is up against.

From LSD in the 1960s to PCP in the 1970s, chemists have long tinkered with illicit substances to thwart the law and produce tailor-made effects. The most famous designer was Augustus Owsley Stanley III, who manufactured high-grade LSD in the Haight-Asbury of the mid-1960s. Owsley, as he was known, was finally arrested in 1967. He was last seen making jewelry in rural Australia.

Fentanyl was developed in the early 1960s by Janssen Pharmaceuticals, a Belgian firm. In its pure form, the drug is a short-lasting analgesic 100 times more powerful than morphine. Marketed as Sublimaze, it was introduced in 1968 to the United States, where it is now used in 70 percent to 80 percent of surgical operations.

In the late 1970s, race-track veterinarians noticed that thoroughbreds were being doped with fentanyl so they would run faster.

At the same time, fentanyl derivatives began appearing in California as "China White," a high-grade Southeast Asian heroin. California, home of 20 percent of the nation's heroin addicts, was ripe for the drug. It took more than a year to outlaw synthetic China White.

About one-fifth of California's addicts are now using fentanyls. Many think they are taking powerful heroin, but increasingly, users ask for synthetics.

"The word on the street about the analogs is they're much more potent than heroin and they seem to last longer," said Darryl Inaba, who runs the Haight-Asbury Drug Detox Project in San Francisco.

Otherwise, the high is identical to heroin's, and the drug is just as addictive.

The first known overdose was in December 1979. Soon, the deaths were happening at the rate of eight to 10 a year.

Then in 1983, 3-methyl-fentanyl appeared on the street sold as Persian White, the world's finest heroin. It cost as much as $350 a dose. It was 1,000 times more powerful than heroin. Forty-nine people overdosed in California, more than had died from synthetic heroin in all the previous years combined.

"This is a sort of your basic street research for profit with indifference about what happens to people," the DEA's Haislip said.

Many of the dead were from California's new class of upscale junkies, who use heroin to temper the effects of cocaine. "The distribution pattern is very curious," Henderson said. "It breaks all stereotypes." It's distributed essentially in the suburbs of California. We've never had an overdose case in Los Angeles.

"We find it in small farming communities in California. If somebody wanted to buy it, I'd tell them not to go to ghettos in Los Angeles or San Francisco, because you're not going to find it there."

In the Bay Area, "the people are coming from Marin County," said clinic director Inaba. "They're much more often white, much more often upper middle class, much more often educated."

And much more often dumb about drugs.

"It's new or naive users that are succumbing to the drugs," Henderson said. "They're just buying something that's powerful, and (the overdoses) probably would occur if they were buying high-grade heroin."

The synthetics are so deadly because they are so potent. A street dose contains only an infinitesmal speck—about 50 micrograms, an amount that could be hidden on the head of a pin.

"You could take any of the street samples and send it to a laboratory and they would send it back as food-grade lactose or powdered sugar," Henderson said. 'It's 99.9 percent pure sugar or lactose."

Because the concentrations were minute, medical examiners were baffled by the early deaths. Then, in January 1981, DEA chemists Don Cooper and Andrew Allen identified the first synthetic China White.

"The sample that I received for the original analysis, the laboratory that submitted it said this powder is supposedly killing people but we can't find anything in it," Cooper said from the DEA laboratory in Tysons Corner, Va.

Such "fantastically small amounts" can be detected only by the most sophisticated labs, said Henderson, who developed the first screening test for the drugs.

"The concentrations we're seeing in the blood are parts per billion and parts per trillion," he said.

Drug agents estimate that a single chemist in eight hours could supply the nation's heroin demand for a day. A closet full of the drug could feed the nation's addicts for six months.

Henderson speculates that the supply is now coming from "one, maybe two, very sophisticated labs." Working for two weeks at a time, the labs can produce about 200 grams, enough for 4 million doses. The four or five raw materials, all available on the market, cost "a couple hundred dollars."

DEA chemist Cooper believes the drugs are the work of one man, perhaps a brilliant grad student. Henderson agrees: "He's the Owsely of the '80s."

Cooper speaks admiringly of the "nifty little variations," the sophistication of the syntheses, the uniformity of cutting materials that are "mixed very nicely, no hot spots." A hot spot—a lump of pure material in the mix—could kill.

Overdose isn't the only risk, however.

The first designer drug disaster occurred in 1982. A group of underground chemists in Northern California tried to design a copy of Demerol, a narcotic painkiller less powerful than heroin or morphine. They came up with MPPP. In their batch as a byproduct with a side effect: Parkinson's Disease, a chronic nerve affliction.

"These young addicts had literally frozen up overnight and were totally unable to move or talk," said Veatch, the head of California's drug program. Physicians issued a warning to the heroin community and the faulty MPPP vanished from the streets. Twenty people were permanently crippled and 500 more may eventually develop the disease.

Officials believe the contaminated drugs may have been manufactured by a man who was arrested in Brownsville, Texas, in October. In the clandestine lab of 50-year-old San Jose attorney Roberto Calunga Garza, who pleaded guilty to charges of manufacturing, distributing and possessing PCP, authorities found illegal drugs as well as defective MPPP.

"Most of the people we talked to thought they were buying heroin," said Dr. Paul Garbe, an epidemiologist at the federal Centers for Disease Control in Atlanta. "These drugs haven't even been tested on animals. Nobody knows what kinds of effects they're going to have on humans."

And nobody knows where the laboratory ingenuity will lead.

[From the Greenville (SC) Piedmont, Mar. 14, 1985]

DESIGNER DRUGS—CHEMIST CREATES DEADLY COMPOUNDS

WASHINGTON.—A phantom chemist in California is foiling authorities by tinkering with molecules to create legal "designer drugs" that adicts say are as strong as heroin but that have killed at least 85 people.

"He's clearly a state-of-the-art chemist," said Gary Henderson, a pharmacologist at the University of California at Davis, who coined the term "designer drugs."

"He'd have to be or he'd kill himself making this stuff. It's that potent."

Drug laws define illegal drugs by their exact molecular structure, so it is possible for the chemist to evade the law by making minor changes in the substance's molecules.

By the time scientists decipher the structure of the chemist's latest product and enforcement agencies take steps to outlaw it—which can consume several months—the phantom chemist simply redesigns the molecule.

Although all of the deaths have occurred in the West, drug officials and chemists say it is only a matter of time before designer drugs spread nationwide.

The mystery chemist is known to have produced 10 variations of the drug fentanyl, widely used as an anesthetic in surgery, but otherwise illegal. Fentanyl has the same effect as heroin or morphine, and addicts can switch freely back and forth, but it is far stronger than heroin and therefore must be cut to a greater degree for street sales.

Only two of the variations of fentanyl have been outlawed. Pharmaceutical industry researchers have produced an additional 210 variations, none of which ever reached the market, and hundreds more theoretically are possible.

"Whoever this guy is, he's obviously got some chemical training and he's got a good laboratory," said Donald Cooper, a chemist who has analyzed the phantom chemist's products at the U.S. Drug Enforcement Administrations laboratory near Tysons Corner, Va. "There are good indications he's cognizant of our legal efforts and he's trying to stay one step ahead of us."

"If this thing breaks out of the West Caost, we hate to think what could happen," said Ronald Buzzeo, deputy director of the DEA's office of diversion control. "We don't have the legal apparatus to really go after this kind of thing. We're looking at ways to control these drugs as a class, but the lawyers say it's not clear we can."

The problem is how to write a definition broad enough to include the whole fentanyl family without being so broad that courts consider the law too vague.

[From the Palo Alto (CA) Peninsula Times-Tribune, May 3, 1984]

"DESIGNER DRUGS"—DANGEROUS, BUT NO LAWS AGAINST THEM

(By Thomas G. Keane)

Drug addicts and dealers on the Peninsula are attempting to escape the law by trafficking in snythetic "designer drugs"—compounds that are not illegal because they do not contain controlled substances, narcotics officers say.

The narcotics are manufactured in laboratories by chemists, who can alter the molecular structure of a particular drug to create a new one that is technically not against law, chemical experts say.

In the past two weeks, agents from the San Mateo County sheriff's Special Investigations Unit have arrested about 20 people in the East Palo Alto area who were allegedly involved in distributing "China White," a heroin substitute that contains a few controlled substances and is illegal. As a synthetic heroin, it has the same narcotic effect as the heroin extracted from an opium plant, only it is produced in a laboratory and is about 100 times more powerful.

However, much to the frustration of U.S. Drug Enforcement Agency officials, many synthetic variations of China White are not illegal.

"It's one of the 'designer drugs,' " said Ian Irwin, a chemist researching a synthetic heroin derivative at Santa Clara Valley Medical Center in San Jose. "Many of its forms aren't listed or controlled; technically, there aren't any laws on the books for them."

According to narcotics agents and chemical experts, China White has been seen on and off the Bay Area drug circuit for about two years.

Parmacologist Gary L. Henderson said the China White series comes from fentanyl, a synthetic analgesic commonly used as a painkiller during surgical operations. The street name "China White" comes from its apparent similarity to a high-grade white heroin imported from Asia.

Sublimaze, fentanyl's trade name, is used in about 70 percent of the operations performed in the United States, he said.

"During the last few years, people are synthesizing (fentanyl)," Henderson said. "They're making very simple analogs of it by taking the molecule structure and making minor alterations."

Henderson, a dean at the University of California at Davis Medical School, is California's expert on synthetic heroin. Police officials and coroners, sometimes unable to identify a drug, will send samples to Henderson, who has the only laboratory outside the Drug Enforcement Agency that regularly tests for China White.

In the past four years, he has analyzed more than 300 samples sent to him by county coroners and identified 40 deaths due to a fentanyl overdose.

Henderson said two fentanyl derivatives are illegal. But he said the list of derivatives is "endless," a fact of chemistry that makes it very difficult for the law to keep up.

Since an entire class of drugs cannot be designated illegal by the government, each derivative must first be tested and demonstrated to be harmful and addictive. The problem, Henderson said, is that once the government outlaws one derivative, the dope-concocting chemist can contrive another one.

"I believe very strongly, for a number of reasons, that there is a very strong movement toward abusing synthetic drugs," Henderson said. "Even with all the efforts to put restrictions on drugs of abuse, for a few hundred dollars and a few weeks you could probably have a supply (of synthetic drugs) that will take three years to sell.

"It's getting to be high-tech war between the dealers and the enforcers."

Addicts are often the casualities of the war. "The dosages are so tiny," Irwin said, "that even a minor error in a few micrograms could cause death."

According to Irwin, the Santa Clara Valley Medical Center has admitted about 100 addicts in the Bay Area during the past year who were exposed to a fentanyl derivative. Because the drug contained a deleterious element, the users devleoped symptons seen in Parkinson's disease patients—slowness of motion, severe mucele rigidity and tremors.

San Mateo County sheriff's Sgt. Alan Johnson said persistent raids have forced the Peninsula source of China White "into remission until the heat dies down." He said since the pressure was applied to one source in San Jose, China White seems to have disappeared from the Peninsula drug market.

Spokesmen from the Drug Enforcement Agency in San Francisco and the Santa Clara County narcotics enforcement team said synthetic heroin has not been as prevalent in drug circles as it was about a year ago.

Still, few would dispute its presence. A supervisor in a San Mateo County drug rehabilitation clinic said the amount of snythetic heroin is probably the same. Henderson estimates that synthetic drugs now make up about 10 to 20 percent of the California drug market.

"DESIGNER DRUG" LINKED TO PARKINSON'S—MPTP DISCOVERY SUGGESTS POSSIBLE CAUSE, PREVENTIVE MEASURE

(By Larry Thompson)

At least 400 northern California drug abusers appear to have taken a synthetic form of the drug Demerol which can destroy a portion of the brain and cause Parkinson's disease in young people.

Newer versions of the drug—which may also prove poisonous—are still being produced in clandestine laboratories, said Dr. A. James Ruttenber, an epidemiologist with the Centers for Disease Control in Atlanta.

The drug may be spreading to other parts of the country, Ruttenber says. Materials and instructions for making the synthetic drugs were found in two clandestine labs in San Diego and one in Brownsville, Tex.

Ruttenber reported the CDC's preliminary findings at the first national "Symposium on MPTP" last week at the Uniformed Services University of Health Sciences in Bethesda.

MPTP, which comes from the same family of drugs as Demerol, caused an epidemic of Parkinson's disease among young drug addicts in the San Francisco Bay area after it was sold as a synthetic heroin in 1982. Its discovery caused an explosion of research into the cause and basic neurology of Parkinson's disease, a degenerative syndrome that strikes people in their fifties and sixties. It causes slowed movement, tremor, rigidity, dementia and death. There is no cure, although the symptoms can be relieved with a drug called L-dopa.

A similar epidemic struck narcotic abusers in the Netherlands in late 1981 and early 1982. Forth-three developed symptoms; 11 died.

The MPTP experience in California and that of another synthetic heroin called fentanyl also has focused federal attention on trying to find a way to stop clandestine laboratories from producing so-called "designer drugs."

Currently, it is legal to make drugs like MPTP because the underground chemists design them to be slightly different from related drugs which are regulated, said Miriam Davis, an adviser to the assistant secretary for health in the Department of Health and Human Services. The modified versions remain similar enough to the active, regulated drugs to produce a narcotic effect.

Entire families of related drugs have not been regulated because "we were concerned about the effects on basic research and on drug research, both in industry and the university," Davis said.

But new legislation is now being developed "that would prohibit designer drug manufacture and at the same time not inhibit research or drug and chemical manufacture," Davis said. She declined to describe the legislation because it currently is being reviewed by HHS and the Department of Justice, but she did say it could be introduced in Congress as early as this summer.

The MPTP story, which began in 1982, is an example of the dangers caused by designer drugs. An underground San Francisco Bay area drug laboratory was making a synthetic drug similar to Demerol when the chemical reactions went awry and produced MPTP as a contaminating byproduct. Since these labs don't perform quality control tests, the drug, containing the MPTP contaminant, was sold on the street.

The effects of MPTP damage were first discovered in July of that year when county sheriffs carried a paralyzed, 42-year old herion addict from jail to the Santa Clara Valley Medical Center in San Jose. While awaiting a hearing, the man had slowly lost his ability to move. Over the next weeks, six more similarly paralyzed drug users were discovered.

Dr. J. William Langston, the medical center's chief of neurology, saw the paralyzed addicts and through a series of lucky breaks and persistent detective work, determined—with the help of Stanford University chemist Ian Irwin—that the compound MPTP had damaged the brain.

The first known case of MPTP poisoning occurred in 1976 when a Bethesda college student made synthetic drugs in his basement for personal use. He, too, apparently produced MPTP as a contaminant and developed the symptoms of Parkinson's disease. He killed himself before National Institute of Health researchers were able to identify the drug.

Once Langston realized that MPTP produced brain damage similar to Parkinson's disease, he used L-dopa to reverse the paralysis of the California addicts.

A few months later, Dr. R. Stanley Burns, a neurologist at the National Institute of Mental Health, showed that MPTP caused a Parkinson's-like condition in monkeys and created the first animal model for the disease.

While the discovery of MPTP has not provided a new treatment for Parkinson's disease, it has suggested a possible cause.

Langston and Dr. Donald B. Calne from the University of British Columbia in Vancouver suggested that Parkinson's disease may be caused by an environmental chemical similar to MPTP.

Langston and Calne hypothesize that the toxin kills some of the brain, but does not produce Parkinson's until aging naturally eliminates key remaining nerve cells gradually. When fewer than 20 percent of those nerves remain, the person develops the disease.

No MPTP-like environmental contaminant has yet been found, although several laboratories are now looking. Other researchers, however, have expressed doubt that Parkinson's is caused by environmental chemicals similar to MPTP.

Langston and Calne are now trying to test their hypothesis by sending California addicts—both the original seven who were paralyzed and others identified by the CDC—to Vancouver, where Calne's group can study the dopamine distribution in their brains with Positron Emission Tomography (PET).

The initial scans show that dopamine distribution is equally reduced in the brains of both drug addicts and older Parkinson's patients.

Calne's group plans to scan the brains of the California drug addicts—both the severely damaged and those who have no symptoms but who used MPTP—on a regular basis for several years, perhaps decades, to determine whether their brains continue to lose dopamine and develop Parkinson's. If that occurs, it will strengthen the environmental cause hypothesis.

CDC's Ruttenber said his group is trying to get institutional support to follow these damaged addicts "for the rest of their lives. . . . It is going to be expensive, but if you are doing all this research on animal models, and you don't know what the natural history of the disease is, you are going to be lost."

Much of the recent research reported during last week's symposium tried to explain why MPTP poisoned the brain and how it selectively killed the dopamine-producing cells associated with Parkinson's disease.

Researchers now believe that MPTP itself is not poinsonous, but that the brain converts it into MPP-plus, an extremely toxic compound similar to paraquat, a herbicide used to destroy marijuana plants and which causes lung damage when contaminated marijuana is smoked. Reportedly, MPP-plus was once tested as an herbicide.

An enzyme call monoamine oxidase (MAO) controls the conversion of MPTP to MPP-plus. By blocking the MAO enzyme with another drug, monkeys experimentally injected with MPTP could be protected from its ill effects.

Dr. Joussa B.H. Youndim from the Technion-Israel Institute of Technology in Haifa, Israel, reported on a study at the Lainz Hospital in Vienna, Austria, that showed Parkinson's patients lived 15 months longer and their disease progressed more slowly when they received the MAO inhibitor deprenyl.

A number of researchers cautioned that the Vienna study was not controlled trial. "I think that particular piece of work is fascinating, but not entirely convincing," said Dr. C. David Marsden, chairman of neurology at the Institute of Psychiatry, Kings College Hospital, London. "There is enough doubt about what deprenly might actually do. It might not only be good, but it could actually be bad."

[From the Santa Ana (CA) Register, Feb. 13, 1985]

"DESIGNER DRUGS": MENACE OF A DECADE

(By Franklin O'Donnell)

"Super cocaine," the man who sold it to them called it.

The young Laguna Beach couple bought a gram of the stuff, a gumstick-sized foil wrapper of white, powdery crystals just ample enough for a party for two. Back in their living room, they fashioned it into lines, leaned close and snorted it. And waited for the rush.

She went into the bathroom. He passed out.

When he came to, the young man went to the bathroom to see where his girlfriend was. He found her dead on the linoleum floor.

Hours later, in a second-floor laboratory overlooking Santa Ana's municipal stadium, chemists in the Orange County sheriff-coroner's office were gingerly analyzing the few stray crystals left on the scrap of foil. "This whole lab was going crazy," Robert Cravey, the sheriff-coroner's chief forensic toxicologist, recalls of the mid-1970's case. "We were working 'round-the-clock' just trying to figure out what it was."

Unlike natural cocaine, the stimulant extract America's coca plant, these white crystals didn't separate chemically when they were supposed to. The lab crew tried their gas chromatograph, a sophisticated machine that excels at tracking down nitrogen-laced compounds such as Valium. They tried their ultraviolet spectrophotometer, a device that scans the chemical footprint left in a spectrum of light when molecules are broken down. The results, Cravey remembers: "Nothing."

Finally, the sheriff's chemists turned to their mass spectrophotometer, another machine that analyzes chemicals by gauging the lines they cast across a light spectrum. The footprint they discovered wasn't in their own library of drugs, but eventually it turned up in a library supplied by the spectrophotometer's manufacturer. "Super cocaine" was a synthetic drug called pro-paracaine.

From an underground chemist's clandestine lab? Not quite; it was eventually traced, Cravey says, to a disenchanted employee of an Orange County pharmaceutical company who took a kilo of the drug along when he was fired.

No matter who makes them, pro-paracaine and other chemicals are a kind of illicit drug that, unlike heroin, cocaine or marijuana, can't trace their heritage to a living plant. Some make their way to the street from a pharmaceutical house or from industry. Others are the stew of underground chemists who tinker with drug recipes to create heroin or cocaine act-alikes. And, because of loopholes in their precise makeup, many are technically legal.

If they succeed in engineering a "designer drug"—tossing in an oxygen atom here, a methyl group there—underground chemists "stay a year or two ahead of the law," says Dr. Sidney Cohen, a UCLA emeritus professor who pioneered work studying LSD.

A smattering of cases from the past decade:

Around 1980, Orange County law officers made several arrests for "11550," the Health & Safety Code statute that, among other drugs, makes the animal tranquilizer PCP illegal. Though the suspects acted as though they were on PCP—known on the street as angel dust or krystal, the drug causes jerky movement and aggressive behavior—chemical tests showed they were high on PCP-y, a legal chemical sibling. The suspects were released.

Two corpses that showed up at the Orange County morgue a few days after Christmas 1979 seemed to be classic heroin overdoses—but, to analysts in Cravey's toxicology lab, the chalky stuff the dead men had shot up looked for all the world as if it was sugar powder. In time, chemists found the powder held minute amounts of alphamethyl-fentanyl, a heroin act-alike that, because of an extra carbon atom and three hydrogen atoms, was completely legal. And, because of its extremely powerful nature, lethal.

In 1977, a 23-year-old grad student in chemistry on the East Coast tried to make a batch of MPPP, a synthetic narcotic much like Demerol, for his personal use. Soon, even when not using the drug, he had difficulty speaking and walking, symptoms that were similar to Parkinson's disease, a brain-damaging malady that usually afflicts only the elderly. Investigators later concluded, says Cohen, that several of the student's drug molecules went wrong; the young man inadvertently invoked Parkinson's disease by chemicals.

Alternative newspapers in Los Angeles and Seattle recently have announced the arrival of XTC—or "Ecstasy"—a chemical relative of MDA, the stimulant-hallucinogen hyped on the street as a "love drug." No cases have reached the state's chief drug labs yet, but criminalists suspect it may be methylene-dioxymethamphetamine, a designer drug that, because of an extra "meth," is technically legal.

On the face of it, the chemistry of "designer" drugs—synthetic chemicals made-to-order to mimic natural narcotics and stimulants—is simple. According to Tom Abercrombie, a chemist with the California Department of Justice's drug lab in Riverside, it's a matter of taking a well-known drug molecule and linking a chemical add-on or two. In some cases, underground chemists do it for enhanced effects; sometimes, it's a bargain to them because the process is cheap. And, many times, they create a substance that's legal.

PCP, for example, is itself a synthetic drug; it's built around a chemical called piperidine, a controlled substance used in making rubber and plastics. "If you start with a different chemical, pyrrolidine," says Abercrombie, "you end up with what's called PCP-y, or sometimes, PHP." In 1979, the chemical difference was enough to let a handful of Orange County users off the legal hook; since then, pyrrolidine and PCP-y have been made illegal as well.

Heroin has its own act-like designer drugs, chemicals built around a synthetic compound called fentanyl. "There are any number of analogs (different versions) of fentanyl that can be synthesized," says Gary Henderson, a UC Davis pharmacology professor who originally coined the phrase "designer drug." Henderson has a contract with the state to monitor the heroin-mimicking drugs.

Doctors, he says, use fentanyl during surgery as an anesthetic; it kills pain during surgery without making the patient unconscious. Underground chemists have taken it from there by adding extra molecules—a little fluorine here, a carbon-nitrogen set there—to create chemical neighbors that, for a time, are legal.

"It's a complete substitute for heroin," says Henderson. "It's extremely difficult to detect because a minute amount goes a long way. And though all the fentanyl analogs are similar, they're completely unrelated to heroin. If a lab isn't specifically looking for it, it's difficult to get to."

Once the law catches up with a particular version of fentanyl, says Henderson, underground chemists switch the formula and try another. Law, rather than chemistry, is what bedevils drug officials most.

"It's a definite enforcement problem," says Christine Flynn, a Sacramento staff member of the state's Division of Alcohol and Drug Programs. "The (underground) manufacturers are very sophisticated; they can make alternate versions of drugs very quickly."

For those underground chemists, the game means playing keepaway with the law, always a few months ahead of drug legislation. Under current law, drugs are controlled chemical by chemical; if a designer drug is off by a few molecules, it's effectively legal.

That—and their chemical unpredictability—has some officials concerned. Robert Roberton, chief of the state's alcohol and drug programs, sees designer drugs as the chief menace of the late '80s.

"They could create a major social disaster," says Cohen, of designer drugs. The UCLA emeritus professor is among drug authorities who want to change the law so broad drug categories—rather than specific compounds—will be declared illegal.

Not everyone agrees. "I suppose it could be argued," says Carole Sidebotham, supervising criminalist for the Orange County sheriff-coroner's office, "that you could lose research in valuable drugs—that it would be more difficult to study drugs for legitimate use."

For the time being, the federal Drug Enforcement Administration does what it can with "scarce" resources, according to Bobby Sheppard of the DEA's Los Angeles office. "Obviously, if there is a drug widely abused and not on the list of controlled substances, then Congress must be alerted," says Sheppard. "But if someone is manufacturing something that is not illegal, we won't go after them."

And though they appear from time to time—and, if some authorities are correct, will emerge increasingly in the late '80s—"designer" drugs as yet seem to be rarities in locales such as Orange County. "We're a rich county, we can afford cocaine," says Dr. Phil Edelman, a pharmacologist who monitors overdoses at UC Irvine.

"There's already a surfeit of heroin and cocaine out there," says Dr. Mike Stone, medical director of Care Unit of Orange, a private hospital that treats a variety of drug addictions. "For the users it's a question of, like, why try this elixir of alcohol-something-or-other from South America when you've got plenty of just plain beer?"

[From the Fort Lauderdale (FL) Broward Review, Apr. 22, 1985]

"DESIGNER DRUGS" MUST BE STOPPED

The legal killers, laboratory products easily formulated and manufactured even by home chemists, already have killed about 90 persons across the United States.

While the drugs currently are in use mainly in California, there is no reason to believe that their use will not eventually spread across the country, with even more tragic results.

Designer drugs—synthetic narcotic analogs—created by slightly changing formulas of some legal and some illegal substances, are, in many instances, beyond the reach of the law, since they are new "products" not yet listed in the registry of controlled substances.

The drugs are so easily manufactured that experts have said one chemist, working eight-hour days, using some of the more potent formulas, could supply the entire nation's heroin demand on an ongoing basis. A $500 investment in chemicals could produce a $2-million batch of the synthetic narcotic.

There's no doubt in my mind that organized crime, always alert to possibilities to profit from the misery of others, will waste no time realizing the evil gains to be reaped from manufacturing these deadly chemicals for sale on America's streets.

For that reason as much as any we urge the National Drug Enforcement Policy Board to develop a strong U.S. policy to deal with this newest generation of deadly drugs. We agree with Chiles that this should be the board's first priority.

[From the Morristown (NJ) Daily Record, May 5, 1985]

DESIGNER DRUGS PERFECTLY LEGAL, BUT VERY DEADLY

(By Jeff Leen)

The drug, 1,000 times more powerful than heroin, is designed in a clandestine lab by a renegade chemist, a brilliant phantom who has earned the grudging respect of law enforcement pharmacologists.

It is cut innumerable times and passed off as Persian White, the caviar of heroin. It is sold in the redwood suburbs north of San Francisco to chic young professionals, junkies in hot tubs.

CHEAP, ADDICTIVE, LEGAL

It killed 49 people last year. It is cheap, addictive and perfectly legal.

By tinkering with the molecular structure of fentanyl, a synthetic painkiller routinely used in surgery, the unknown chemist has created the latest fad to come out of California— "designer" heroin.

"We're talking about a world-class medical chemist," said Dr. Gary Henderson, a pharmacologist at the University of California at Davis who coined the term "designer drugs" for the synthetic substances that began cropping up on the West Coast in the late '70s.

"First they said it was California craziness, 'It's going to go away.' I don't see it. Something that's 1,000 times more powerful than heroin, dirt cheap to make, hard to detect, you can smoke it, snort it, you don't have to inject it."

UNIQUE PROBLEMS

The state-of-the-art drug poses unique problems. Coroners cannot detect it in overdose victims. And there is a laboratory loophole that could endlessly frustrate the law:

New variations can be turned out faster than they can be identified and outlawed. And when they are finally made illegal, a sophisticated "designer" can create a new, legal drug merely by altering the molecule. The users are the guinea pigs.

"This is very, very frightening," said Chauncey Veatch, director of the California Department of Alcohol and Drug Programs, which expects 78 people to die this year from designer drug overdoses.

To date, 90 people have died from such overdoses, 13 this year. The fear is that the new heroin will sweep the country. Three designer drug deaths have occurred outside California, two in Oregon and one in Arizona.

"As California goes, so goes the rest of the nation. That's what happened with LSD," warned Frank Chellino, U.S. Drug Enforcement Administration spokesman in Miami, Fla.

FEDERAL ATTENTION

Last Month, U.S. Sen. Lawton Chiles, D-Fla, proposed legislation that would focus federal attention on the problem.

"This will come out of California and, look out, it'll come across fast," Chiles said. "It's so easy to produce these drugs in small labs: A $500 investment in chemicals can produce a $2 million batch of synthetic heroin. There's just too much money there. It's just got to spread."

Henderson said he has heard that underground chemists are going to California to learn how to make fentanyl.

Right now, law enforcement can do little. If DEA agents raided a designer drug lab tomorrow, chances are they couldn't make any arrests.

"I think (arrests would be) very doubtful," said Gene R. Haislip, director of the DEA's office of diversion control.

ILLEGAL IN 30 DAYS

It used to take months, even years, to list a drug—by chemical formula—in the Controlled Substances Act. "We can't take action based on a suspicion. We have to have data," Haislip said. Now, under legislation passed last year, a drug can be made illegal in 30 days.

Thirty days is still plenty of time for a smart designer to change the formula.

[From the Tampa (FL) Tribune, Apr. 1, 1985]

"DESIGNER DRUGS" POSE WRETCHED NEW THREAT

The latest development in the drug trade is the emergence of "designer drugs," substances with slightly altered molecular structures that are offered as substitutes for heroin and other narcotics.

They have been described as easy to make, deadly in use—and beyond the reach of law enforcement agencies.

Until a particular drug is classified as a controlled substance by the state or federal government, it remains legal both to make and use.

Lawton Chiles, Florida's Democratic senior senator, is proposing legislation he hopes will mark the beginning of a fight against this growing threat.

His bill would direct the National Drug Enforcement Policy Board and the Office of Technology Assessment to examine the "designer drug" menace and recommend steps to curb it.

Sen. Chiles has observed that these custom drugs can be developed and produced faster than they can be identified and outlawed.

"Even with the emergency scheduling provisions of the Controlled Substances Act, the clandestine labs can always stay beyond the reach of the law with a slightly different compound that is not yet on the schedule of controlled drugs," Chiles said.

He is absolutely right, but that only tells part of the story. The "designer drugs" can be synthesized at an extremely low cost. For instance, $500 worth of chemicals and equipment can produce a cup of the heroin substitute, "China White," that would be worth $2 million on the street.

That this drug has been responsible for the deaths of 65 heroin users in California and has caused serious brain injuries in more than 200 others has not discouraged potential "consumers."

Nor is the heroin substitute the only drug to emerge from clandestine laboratories. Such labs have also produced LSD, PCP, amphetamine and methaqualone, among others.

Almost every drug currently classified as illegal can be made legal by modifying its molecular architecture. Experience has demonstrated conclusively that it doesn't take long for these products to move from the more sophisticated users in the drug culture to the street where they become even more dangerous in the hands of young, inexperienced people experimenting with artificial highs and lows.

Sen. Chiles offers no answer to the problem, but he wisely suggests that one is urgently needed.

The drug problem is one of the nation's principal agonies, not only because it weakens society in a multitude of ways but because it seems to defy solution. Now, with the emergency of "designer of drugs," that problem can only markedly worsen.

Can a democratic society control a menace that is so extraordinarily convoluted, ubiquitous and profitable?

The shape of American life in the years ahead hinges on the answer.

"DESIGNER DRUGS"—POTENT SYNTHETIC NARCOTICS, READILY TAILORED IN A WIDE ARRAY OF CLANDESTINE ANALOGS, COULD BE HARBINGERS OF AN ALARMING NEW TREND IN DRUG ABUSE

In 1979, an unfamiliar and uncommonly potent new drug surfaced among heroin users in southern California. So novel was its nature, and so miniscule the amounts needed to kill, that its chemical structure managed to elude expert forensic chemists for some weeks. Eventually the drug was identified, its abuse potential documented, and its unauthorized use outlawed. The drug began to disappear from the streets and today there is little evidence that it has returned in any significant amounts.

That is not the end to the story, however, because as the supply of the original drug dried up, it was replaced with a chemical cousin—one of many equally-deadly analogs. The new variant possessed an important advantage that its predecessor no longer retained. As a new and chemically unique entry in the underground pharmacopia, it was not yet illegal and could, for at least another several months, be safely trafficked without threat of criminal penalty.

Some nine months later, the second version too made the list of federally controlled substances, but it was soon replaced by yet a third analog. The cycle, once again, is progressing to a somewhat predictable conclusion. Welcome to the era of "designer drugs"—synthetic drugs so new to the streets that most have not been declared illegal, and so readily tailored in an enormous variety of distinct chemical designs that their control appears virtually impossible by current methods.

The prototype for this unsettling trend is a family of potent narcotics consisting of fentanyl and its analogs. Although they are usually passed-off as "China White" or other high-quality forms of heroin, these entirely man-made chemicals, in fact, pack a much stronger punch.

"It looks like heroin, feels and tastes like heroin, and kills you like heroin," said Gary L. Henderson, Ph.D., Associate Professor of Pharmacology. The action of the fentanyl compounds is pharmacologically similar to heroin as well, but because of their extreme potency (25x greater than heroin, or 200x that of morphine) it is far easier to overdose and rapidly slide into coma and respiratory arrest, he said. By some accounts, fentanyl overdose victims can go out so fast, they are occasionally found dead with the needle still in their arms.

Henderson, who is considered a leading authority on the fentanyls and their metabolism, has studied the pharmacokinetics of the parent compound in humans and animals since 1972. Collaborating with him in his early studies were John Eisele, M.D. (Prof., Anesthesiology and Human Physiology) and Eliezer Benjamini, Ph.D. (Prof., Med. Microbiology).

Originally developed as an analgesic, fentanyl itself is legitimately marketed under the trade-name Sublimaze (Janssen Pharmaceutica, Inc.) and distributed in liquid form in small glass ampules. according to Henderson, however, the powdery street versions of the fentanyl family are of decidedly clandestine manufacture.

The drug, or any of its hundreds of potentially active analogs, is relatively easily made from inexpensive, readily available materials. "There are essentially only three or four steps to produce the final product," said Henderson. "It requires a chemist, but not a terribly sophisticated chemist, to make it. "Unlike the more time-consuming production of actual heroin from opium poppies, sizeable factories aren't needed to make fentanyl in financially lucrative quantities—a factor that further complicates effective law enforcement. "In a single weekend, it would be possible for a saavy chemist to make a two or three year supply worth $2-3 million," he said. "I doubt that many factories for making the materials will ever be found."

Ironically, the potency that makes the fentanyls so dangerous if not properly cut or diluted may also contribute to their growing popularity. Because so little goes such a long way, the drugs are easily concealed and transported in small quantities, making them potentially popular in prision and other populations. The quantities of the drug that were recovered from some of the first fentanyl overdose fatalities weighed less than a postage stamp and, even then, were less than 0.1% pure.

Detecting what is still a relatively obscure street drug in such minute quantities can prove exceedingly difficult after autopsy. Because it is chemically unlike the more common opium-based narcotics, it is not picked up by standard analytical methods. Although some cases may have been overlooked in the past, coroners and drug abuse officials in California are increasingly sending samples to Henderson when they suspect drug abuse but come up empty-handed in their own analyses.

Outside of the facilities of the U.S. Drug Enforcement Agency, Henderson's UC Davis lab is the only one in the state set up to detect and quantitate fentanyl and related compounds in samples or body fluids. "It's present in such small amounts in the body that it's difficult, if not impossible to detect by conventional laboratory methodology," explained Henderson.

As a result of their early studies, Henderson and his colleagues developed extraordinarily sensitive radioimmunoassay procedures for following the disposition of fentanyl (Sublimaze) and its metabolites in body fluids. Consequently, as the distribution of "synthetic heroin" began to spread, the state's Department of Alcohol and Drug Programs two years ago asked Henderson to modify that assay procedure to enable the routine detection of alpha methyl fentanyl (then the dominant analog in circulation) and possibly other analogs with abuse potential.

"The essay procedure we developed relies on manufactured antibodies to specifically identify the drug molecule. The procedure is sensitive enough to pick it up in nanogram (one billionth of a gram) quantities," said Henderson. Unfortunately, the powerful specificity that makes such a sensitive test possible, also prevents its use as a broadspectrum assay for all of fentanyl's many derivatives. "Our procedures are good for some analogs, but work less well for other analogs and the metabolities." Consequently, a battery of related analytical procedures eventually may be required to keep up with the growing catalog of illicit fentanyl compounds.

Since the era of designer drugs dawned four years ago, Henderson's laboratory has analyzed over 300 samples sent to him from coroners, drug abuse programs and law enforcement agencies in California. To date, he has attributed 32 deaths of fentanyl overdoes. New samples continue to arrive for testing at the rate of two or three per week.

Recently, the UC Davis pharmacologist discovered the third, and latest, analog in the "China White" series. Tentatively identified as an acetyl methyl analog, the still-legal drug follows on the heels of recently outlawed parafluoro fentanyl. Although he rarely sees the alpha methyl analog—the original synthetic heroin—anymore, Henderson reports that, surprisingly, some samples of the already controlled fentanyl parent compound also have appeared recently.

Another, perhaps more disturbing, trend noticed by Henderson and others has been the spread of synthetic heroin from its original geographical base in southern California and Arizona. Its move northward was signaled by a cluster of cases months ago in Monterey County. Most recently, four to five overdose victims have been identified in the Sacramento area. California still accounts for most of the documented cases, but Henderson suspects that the problem may be growing out-of-state as well.

"The problem is that most people outside California aren't looking for it, so it's impossible to assess how widespread it is," he said, evidencing some frustration. "They haven't taken this problem seriously yet." Henderson also suspects there may be a tendency by out-of-state officials to dismiss fentanyl as an isolated problem among "a few California crazies."

Locally, Henderson is hardly alone in the opinion that the arrival of "designer drugs" (of which the fentanyls are only one possible series) is an ominous sign for the future of society's problems with drug abuse. In the words of one concurring state drug abuse official, "It's frightening because, right now, it's a bottomless pit."

Henderson is concerned that, like so many other problems confronting society, the danger of "designer drugs" may go largely unrecognized and unaddressed until some tragedy brings it truly widespread attention. "I hope it doesn't take the death of someone who is popular and well-known—an entertainer or someone close to a prominent politician—before people really wake-up and take notice," he said soberly.

"DESIGNER DRUGS" SKIRT THE LAW—PHANTOM CHEMIST SOUGHT

(By Boyce Rensberger)

A phantom chemist in California is foiling authorities by tinkering with molecules to create legal "designer drugs" that addicts say are as strong as heroin but that have killed at least 85 people.

"He's clearly a state-of-the-art chemist," said Gary Henderson, a pharmacologist at the University of California at Davis, who coined the term designer drugs. "He'd have to be or he'd kill himself making this stuff. It's that potent."

Drug laws define illegal drugs by their exact molecular structure, so it is possible for the chemist to evade the law by making minor changes in the substance's molecules.

By the time scientist decipher the structure of the chemist's latest product and enforcement agencies take steps to outlaw it—which can consume several months—the chemist simply redesigns the molecule.

Although all of the deaths have occurred in the West, drug officials and chemists say it is only a matter of time before designer drugs spread nationwide.

The mystery chemist is known to have produced 10 variations of the drug fentanyl, widely used as an anesthetic in surgery but otherwise illegal.

Fentanyl has the same effect an heroin or morphine, and addicts can switch freely back and forth, but it is far stronger than heroin and therefore must be cut to a greater degree for street sales.

Only two of the variations of fentanyl have been outlawed. Pharmaceutical industry researchers have produced an additional 210 variations, none of which ever reached the market, and hundreds more theoretically are possible.

"Whoever this guy is, he's obviously got some chemical training and he's got a good laboratory," said Donald Cooper, a chemist who has analyzed the phantom chemist's products at the U.S. Drug Enforcement Administration's laboratory near Tysons Corner, Va. "There are good indications he's cognizant of our legal efforts and he's trying to stay one step ahead of us."

Cooper and other chemists who have been tracking the phantom chemist since 1981, when his products first appeared, have developed a grudging admiration for him. They cite a drug be made called 3-methyl fentanyl. It is about 1,000 times stronger than heroin. The amount absorbed through the skin from a smudge on one finger would be "enough to knock you down," said Henderson.

But, Henderson said, "the stuff he makes is clean and the dose is cut just right. Every time I get a sample from the police, I think about this guy. I wonder what he's got in store for us. It's usually pretty interesting."

Henderson and Cooper are among many who believe it is inevitable that designer drugs will spread east. All the deaths so far have been in California except for two in Oregon and one in Arizona.

Although receipes for making fentanyls are not yet in the cookbook form used by clandestine drug labs making LSD, PCP, amphetamines and other other drugs, Henderson and Cooper worry that a chemically sophisticated person could figure it out from chemical literature.

All but one of the fentanyls made by the phantom chemist are forms described in the chemical literature. One, called para-fluoro fentanyl, was his own invention. Investigators say they believe that only one chemist is likely to be at work because the same combination of other substances is used to cut the drug. This would be unlikely if several chemists were working independently.

"If this thing breaks out of the West Coast, we hate to think what could happen," said Ronald Buzzeo, deputy director of the DEA's office of diversion control. "We don't have the legal apparatus to really go after this kind of thing. We're looking at ways to control these drugs as a class but the lawyers and the scientists say it's not clear we can."

The problem is how to write a definition broad enough to include the whole fentanyl family without being so broad that courts consider the law too vague. "Besides," Henderson said, "no matter how many variations you put in the law, I'll bet I can think up another one."

Although several classes of designer drugs are made in other clandestine labs, fentanyls are the major concern now. Another group, for example, also acts like heroin but causes Parkinson's disease.

Because plain fentanyl is about 80 times more powerful than heroin, dealers usually cut it far more than they do heroin. It is often sold as China White, the usual name for a superior grade of Asian heroin. The 3-methyl fentanyl form is sometimes sold as Persian White, the finest grade of heroin.

Plain fentanyl, like all organic compounds, is a molecule made of several kinds of atoms—carbon, hydrogen, oxygen and nitrogen—linked in a specific configuration of rings, strings and other patterns. The shape of the resulting molecule and the nature of the atoms at various positions determine how it will react in the body.

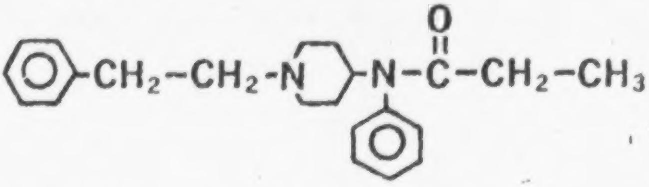
Designer alterations of fentanyl are possible, however, because some points on the molecule can bind to additional atoms or groups of atoms. In the case of 3-methyl fentanyl, the molecule is a plain fentanyl with a methyl group (a carbon surrounded by three hydrogens) stuck on at a position that chemists, by convention, designate as No. 3.

For reasons not understood, this alteration makes the molecule react much more strongly with the nerve cell's opiate receptor sites, multiplying its strength. The alternation also turns the molecule into something other than fentanyl, something legal.

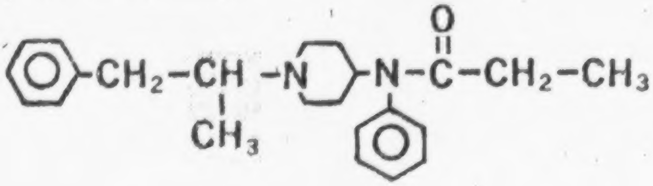
DESIGNER DRUGS

(VARIATIONS IN THE FENTANYL FAMILY)

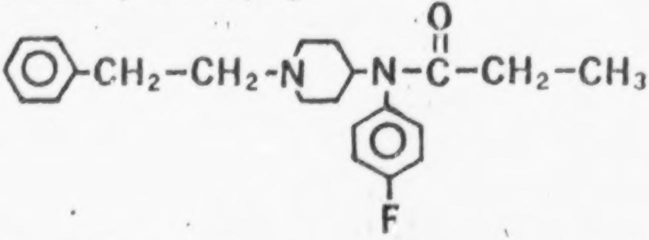
fentanyl--legal only as surgical anesthetic



alpha-methyl fentanyl--illegal



para-fluoro fentanyl--currently legal



Plain fentanyl, top, is a synthetic narcotic, made entirely from industrial chemicals. It consists of linked atoms of carbon, hydrogen, oxygen and nitrogen, indicated by initials. Hexagons are chemists' way of representing rings with carbon atoms at each point and hydrogen atoms sticking out from each carbon unless the carbon is linked to something else. To make alpha-methyl fentanyl, middle, chemists follow a slightly different procedure that ends up with a methyl group (CH^3) attached at one point. Para-fluoro fentanyl, bottom, results from a procedure that binds a fluorine atom to one of the rings.

THE WASHINGTON POST

[From the Christian Science Monitor, June 19, 1985]

"DESIGNER DRUGS" THREATEN TO OPEN A NEW ERA IN DRUG ABUSE

(By Scott Armstrong)

BOSTON.—A new class of dangerous street drugs is emerging.

Some law enforcement officials say they believe it could dramatically alter the nation's war on drugs in the 1980s.

The source of concern: synthetic drugs—substitutes for illegal substances such as heroin that are made by "underground" chemists and are perfectly legal.

So far, the manufacture and use of the most potent of these so-called designer drugs has been limited mainly to California, where about one death a week is now being attributed to them.

But some drug-enforcement experts see in California's experience a portent of what could become a nationwide phenomenon. Morever, recent controversy over the widely used MDMA, a stimulant popularly known as "Ecstasy" and a designer drug that some experts say is relatively benign, has fueled concern that the United States may be entering a new era in drug abuse.

"A year ago I would have said this is quite a small problem," says Gene Haislip, deputy assistant administrator for the US Drug Enforcement Administration (DEA), of designer drugs. "Now events are moving so fast we've had to reassess where we stand.

Particularly frustrating to law enforcement officials are several unusual problems designer drugs pose:

Most are legal. Current laws define illegal drugs by exact chemical formulas. So chemists can skirt regulations by tinkering with the molecular structure of a substance. Thus even if a synthetic drug later becomes controlled, chemists can usually produce slight variants beyond the reach of the law.

They can be potent. Some of the synthetic heroin that has surfaced in California produces the same effects as natural heroin but is several thousand times stronger. This adds to its popularity but also increases the chances of overdoses. It also means a few people can wreak a lot of havoc: California drug enforcement authorities say that some of the synthetic heroin is so potent that one chemist working an eight-hour day could supply the nation's entire daily heroin habit.

They can be difficult to detect. Because of the small doses needed, synthetic heroin is virtually impossible to trace in a user except with the most sophisticated equipment, which would hamper policing even if the substances were banned.

"I think this is the wave of the 1980s," says Dr. Robert J. Roberton, chief of California's Division of Drugs. "The technology is here to do it."

Producing synthetic drugs is not a new idea. Pharmaceutical firms, for instance, routinely manipulate the atomic structures of compounds to try to come up with new products. But any drug these legitimate chemists produce must go through rigorous testing on animals.

Even synthetic versions of street drugs such as LSD and amphetamines have existed since the 1960s. But the latest wave of synthetic narcotics in California is more pervasive—and is showing a new level of sophistication.

"We've gone from smoking opium to using morphine with a syringe to heroin. Now we are using synthetic opiates," says pharmacologist Gary Henderson, an expert on designer drugs at the University of California at Davis. "It's the same problem we've had for 6,000 years. it's just an escalation in the technology."

"Ecstasy" is currently the most popular designer drug—although it is in a different class than the synthetic narcotics in California and there's even some debate over how harmful it is.

Still, the DEA recently decided to ban the stimulant due largely to research on a similar drug that concluded it can cause brain damage.

The emergency order takes effect July 1 and can hold for up to a year. In the meantime, public hearings and studies are under way to help determine whether the drug should be permanently controlled.

A chemical spinoff of an illegal stimulant called MDA, Ecstasy has long been used in psychotherapy. But it has also become a popular recreational drug among college students and young professionals in the past two years in 21 states.

Some drug-abuse clinics say they have begun to see heavy Ecstasy users showing up with symptoms of depression, anxiety, and paranoia. Ecstasy is also blamed for having caused two suicides.

Its clasification as a "Schedule I" controlled substance limits its use mainly to research, which angers some psychiatrists who consider the drug safe when taken under supervision and insist it should be allowed for medical use at least.

The synthetics currently causing concern in California, meanwhile, represent the most lethal and ominous end of the designer-drug spectrum. So far, 100 deaths have been attributed to overdoses of synthetic heroin, most in the past 15 months. All but three of the deaths were in California. The others occurred in Oregon and Arizona.

California police were first alerted to the problem in 1979, when two addicts died from what was thought to be heroin overdoses. Later, medical examiners said the culprit was a variant of fentanyl, an anesthetic commonly used in surgery.

The spinoff (alpha-methyl fentanyl) was banned in 1981. but by then more than a dozen users had died and a modified version, legal because of its different chemical structure, was already being sold. When the second drug was banned, yet another surfaced. To date, six fentanyl spinoffs have appeared, one 3,000 times as strong as heroin. Police suspect the synthetics are the work of just a few underground chemists, since the lab work involved is so sophisticated.

Currently, an estimated 20 percent of the state's heroin addicts are using synthetics.

The technology exists to fabricate virtually unlimited numbers of synthetic drugs, many of them from cheap and readily available raw materials.

"By the end of the 1980's, addicts will almost be able to order how they want to feel," predicts Dr. Roberton.

But efforts are being made to head this off. The DEA has already been brandishing new powers granted it by Congress last fall in scheduling drugs. Normally it takes up to a year to put a drug on the controlled-substances list. Now the DEA can do it in 30 days.

California lawmakers are mulling over a proposal to control the entire fentanyl family. Similar umbrella laws have been considered at the federal level. But it is difficult to draft laws that will stand up in court: In effect, the measures ban drugs that don't even exist yet.

In Florida, legislation has just been passed giving the state attorney general more power to control designer drugs. In Congress, bills have been introduced in both houses to study the problem.

[From Time Magazine, Apr. 8, 1985]

DEATH BY DESIGN

They look like heroin, they act like heroin, and they satisfy an addict's urge just like the real thing. But when subjected to a chemist's scrutiny, the narcotics that have been flooding California turn out to be something else. They are "designer drugs"—designed, that is, to get around the law.

The drugs are created by underground chemists who tinker with the molecular structure of illegal narcotics to produce variants that are not explicitly banned by federal law. Thus it is legal to make and use designer drugs. But it is by no means safe, as those who toyed with MPTP have learned.

Police in Orange County, Calif., first encountered designer drugs in 1979, when they found two young addicts lying dead near samples of a heroin-like powder. Thirteen more users had died before Forensic Chemist Donald Cooper of the U.S. Drug Enforcement Administration managed to identify the substance. It was a designer version of the anesthetic fentanyl, which is widely used during prolonged surgery. The variant was many times as powerful as heroin; just a little could be an overdose.

The drug was outlawed in 1981, but another modified fentanyl instantly appeared on the streets; when the second drug was banned, a third popped up. So far, six fentanyl-like drugs have appeared, one of them a thousand times the strength of heroin. All told, they have killed at least 90 people.

California authorities believe that 20% of the addicts in the state have used designer dope. And, says Pharmacologist Gary Henderson, an expert on designer drugs at the University of California at Davis, the drugs are now favored by affluent cocaine users as a way of taking the "edges" off coke.

Experts suspect that the designer fentanyls are the work of a single evil genius (who must now be very wealthy; some $2 million worth of drugs can be produced from $200 worth of chemicals). Cooper says that the lab work is so sophisticated that "I just don't think more than one person could be doing it."

DRUG'S CHILLING TERROR—NARCOTIC SUBSTITUTE "FREEZES" VICTIMS INTO LIVING STATUES

(By Arthur Browne)

As demand for "designer drugs" grows, it also is producing an increasing number of overdoses and serious health problems. None is more serious than the damage caused by MPTP—a substance that was sold in California for a short time three years ago as a substitute for heroin.

More than 70 people who injected themselves with the drug have been afflicted with the symptons of advanced Parkinson's disease. Rigid and immobile without medication, they are frozen like living statues. Their chances of recovery are slim.

The story of MPTP emerged in 1982 when a 42-year-old heroin user was brought into the Valley Medical Center in Santa Clara, Calif., suffering from bizarre symptoms.

"Very dramatically, he had completely frozen almost overnight," said Dr. William Langston, chairman of the hospital's neurology department.

"I had never seen a case like it and we began investigating. We then found that his girl friend, who was 32, was in the same condition. She was at home and for two weeks her family had been getting her up in the morning, bathing her, and feeding her three times a day. It was like having a store mannequin in their house."

Langston and a team of doctors at the hospital assumed initially that their patients, whose faces were rigid and contorted, were unconscious. Then the doctors noticed that the man had some slight movement in his fingers and they decided to see if he could write.

"He couldn't make a sound but he could write," Langston said. "We were amazed when he wrote, 'I have no idea what is going on. I just can't move.'"

The doctors were more baffled than ever, but they got a break when one member of their team, Dr. Phil Ballard, met a local neurologist at a dinner party.

"In the middle of dinner the neurologist told about two brothers who were shooting up heroin and had become frozen and would have starved to death if their mother hadn't visited them," Langston said.

A public warning brought seven more cases to light. The physicians then received a phone call from a police technician who remembered reading an article in a scientific journal in the 1970s about a graduate student who had become frozen after injecting himself with a drug he had synthesized in his lab.

The student had been trying to produce meperidine, which is similar to the legitimate, widely used painkiller drug Demerol. But the student had somehow erred and created instead MPTP, a potent neurotoxin.

The doctors also obtained a sample of the drug injected by their patients. It proved to be MPTP.

"Whoever was making the stuff was trying to make meperidine so that he could sell it as synthetic heroin," said Langston. "But it is very hard to make it without getting some MPTP, and a bad batch hit the street."

Langston said MPTP attacks and destroys the same portion of the brain that is attacked by Parkinson's disease. In its milder forms, Parkinson's causes a shuffling gait and difficulty of movement. In severe forms, usually found in the elderly, it brings on total rigidity, and sometimes an "on-off" effect, in which the rigidity comes and goes without warning.

"People will be fine one moment and then frozen the next, as if their medication isn't working." said Langston. "One of our patients who took the MPTP was driving down Highway 1 and ran out of gas. He started to walk along the side of the freeway, but froze. He couldn't even move his arm to wave for help. He stood there for two hours immobile while cars whizzed by. He finally turned on again and got help."

Langston said he has identified approximately 300 people in California—most between 20 and 40—who injected themselves with the MPTP. Some, he said, are only only beginning to exhibit Parkinson's-like symptoms. They are all, he said, "at substantial risk," and the outlook for those with the most severe cases is terminal.

[From the Tacoma (WA) News Tribune, Mar. 14, 1985]

85 DEATHS LINKED TO "DESIGNER DRUGS"

WASHINGTON.—A phantom chemist in California is foiling authorities by tinkering with molecules to create legal "designer drugs" that addicts say are as strong as heroin but that have killed at least 85 people.

"He's clearly a state-of-the-art chemist," said Gary Henderson, a pharmacologist at the University of California at Davis, who coined the term designer drugs. "He'd have to be or he'd kill himself making this stuff. It's that potent."

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The mystery chemist is known to have produced 10 variations of the drug fentanyl, widely used as an anesthetic in surgery but otherwise illegal. Fentanyl has the same effect as heroin or morphine, and addicts can switch freely back and forth, but it is far stronger than heroin and therefore must be cut to a greater degree for street sales.

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"Whoever this guy is, he's obviously got some chemical training and he's got a good laboratory," said Donald Cooper, a chemist who has analyzed the phantom chemist's products at the U.S. Drug Enforcement Administration's laboratory. "There are good indications he's cognizant of our legal efforts and he's trying to stay one step ahead of us."

Cooper and other chemists who have been tracking the phantom chemist since 1981, when his products first appeared, have developed a grudging admiration for him. They cite a drug he made called 3-methyl-fentanyl. It is about 1,000 times stronger than heroin. The amount absorbed through the skin from a smudge on one finger would be "enough to knock you down," said Henderson.

But, Henderson said, "the stuff he makes is clean and the dose is cut just right. Every time I get a sample from the police, I think about this guy. I wonder what he's got in store for us. It's usually pretty interesting."

FROM HEROIN SNAFU: PARKINSON'S MODEL

(By Lawrence M. Prescott)

SAN DIEGO.—An error in an illicit drug laboratory in Northern California has led to the discovery of an animal model of Parkinson's disease.

A mistakenly prepared substance, selectively neurotoxic to the substantia nigra, at first exerted its effects on "human models." It produced a clinical picture in humans remarkably like Parkinson's disease, reported neurologist Phillip Ballard, of the Santa Clara Valley Medical Center, San Jose, Calif., at the American Academy of Neurology meeting.

In a Northern California home laboratory, a "cookbook chemist" tried to make 1-methyl-4-phenyl-4-proprionoxy-piperidine (MPPP), a synthetic heroin sold on the street as China White. But he wound up with a toxic by-product in the synthesis: 1-methyl-4-phenyl-1,2,5,6-tetrahyedropyridine (MPTP). The admixture of MPPP and MPTP was sold to six addicts, who used it intravenously and developed severe parkinsonism.

Ranging in age from 22 to 42 years, the six had a three-month to 14-year history of heroin abuse. After at first feeling "stoned," they almost immediately started experiencing parkinsonian symptoms: slowing, stiffness, myoclonic jerks, and tremors. By the time they checked into the hospital, two to six weeks later, they had the shuffling gait, flexion posture, and severe, quaking immobilization characteristic of the disease. No cognitive impairment was found, however, and lab tests were, for the most part, normal. Only CSF protein was elevated.

All patients responded to carbidopa-levodopa (Sinemet) and the dopamine agonist, bromocriptine. They are still on it.

A colleague of Dr. Ballard's, Dr. J. W. Langton, announced that concurrent animal studies being carried out by Dr. Richard S. Burns at NIH have successfully induced "parkinsonism" in rhesus monkeys, right down to brain lesions in exactly the right place. It even responded to carbidopa-levodopa. The investigators can now explore dopamine deficiency and neurotransmission interruption to an unparalleled degree.

Back in 1979, NIMH neuroscientists had actually seen the effects of MPTP but didn't know what it was. An opiate addict was treated for parkinsonism after sloppily synthesizing a synthetic himself and using it. He was treated on and off at NIMH for 18 months, finally committed suicide, and necrosis in the substantia nigra was verified at autopsy. Only when the California case came to light were investigators able to put their hands on MPTP.

[From the Sacramento (CA) Bee, Apr. 26, 1985]

Legal "Designer Drug" Is Following in Cocaine's Tracks

(By Drew Jubera)

Dallas.—It's here, whether certain people want it to be or not, and it's called Ecstasy. It is not a perfume or a line of jeans. It is a recreational drug—in jargon, a designer drug—that has become the most recent contender for the drug of preference among those for whom fashion and chemical euphoria still rank high on a list of personal priorities.

So far, the street reviews have been raves. How popular Ecstasy has become in Dallas and elsewhere is still hard to guage. For those who have tried it (it's sold in both tablet or capsule form for $20 to $25 per 100-miligram dose), or who run in those circles where it is being tried, the drug over the last several months has at least become a growing phenomenon.

Ecstasy is currently considered somewhat "upscale" and "adult-oriented" in its appeal, in the same manner once attendant to cocaine, though as the drug's popularity has spread, its class and age distinctions appear to have thinned proportionally.

Evilu Pridgeon, a specialist with the drug abuse prevention program at the Dallas Independent School District, says a segment of high school students is believed to be taking it, too. The drug is also particularly atttractive to weekend experimenters, and for one very good reason: According to law enforcement officials, Ecstasy at this point is not illegal.

So what is Ecstasy?

The origin of its silk-hose, sex-laced name is fuzzy, though it generally is believed to come from its laboratory designation, "XTC."

Its legitimate chemical designation is MDMA—methylenedioxy-methamphetamine—and its chemical composition is related both to amphetamines (speed) and mescaline. Its effect, said William Tedford, a professor of psychology at Southern Methodist University, is a combination of a minor stimulant and a minor hallucinogenic, making it "like taking cocaine and LSD together, after having watered them down considerably."

MDMA is also a second cousin of MDA, a psychedelic that in the 1960s and early '70s became known, because of its profound but still workable effects, as "the businessman's LSD." Ecstasy, too, is said by users to leave them with their faculties while getting them high.

Ecstasy was first synthesized, or "designed," by a California biochemist named Alexander Shulgrin. An anonymously published field guide says Shulgrin created the drug during the '70s for the CIA in its search for "the ultimate truth serum," and that MDMA was his contribution.

But Rick Seymour of the San Francisco Haight-Ashbury Free Medical Clinic, said this genesis is dubious, though he did describe Shulgrin as someone "involved in this for a long time, a biochemist interested in these chemicals who publishes his results, and who then synthesizes some more."

Shulgrin could not be reached for comment.

MDMA indeed is used by a handful of psychiatrists across the country in various kinds of psychotherapy. The drug tends to dissolve both psychological and emotional barriers. It has been described by psychiatrists who use it as an aid in helping people "get in touch with feelings ordinarily not available to them," "healing fear" and making it "easier to look at the issues in your life and it brings about a quality of acceptance."

Testimonials to Ecstasy among recreational drug users abound. Their delight with the drug seems less in the windows it opens on to their souls as in what are considered by satisfied users as the drug's two strengths: its gentle kick and mild euphoria, which allow one to feel high without feeling drugged; and the sense-heightening, libidoswelling effect of an aphrodisiac.

"It makes me real happy, like coke (cocaine) does, but it doesn't keep me awake like speed," said one 30-year-old professional who has tried Ecstasy several times. Though Ecstasy at this point is legal, this professional as with other users who were interviewed, asked to remain anonymous.

The drug's popularity also owes something to the fashion sense and eternal search for the Holy Grail—or at least the ultimate drug—of drug users.

"I think people are starting to look for something else," said John Swartz, spokesman for the Drug Enforcement Agency in Houston. "Cocaine is still a trendy drug, but drug users are always looking for something else."

Why is DEA and the Food and Drug Administration currently working to get MDMA classified as a controlled substance, which would allow law enforcement officials to crack down on its use?

For one thing, Seymour said, some kids already are gulping down a half-dozen or more of the tablets in an attempt to make the drug work as an amphetamine. And because the drug is believed to be manufactured in clandestine labs, quality control is non-existent.

There has been no long-term testing of the drug. Taken moderately over a short period of time, Ecstasy so far has shown no substantially negative effects.

[From the Sacramento (CA) Bee, Aug. 30, 1984]

NEW, DEADLY SYNTHETIC DRUG IN BAY AREA

SAN FRANCISCO (UPI).—Fentanyl, a new synthetic narcotic used as a substitute for heroin, has begun to pop up in Northern California street sales with increasing frequency, law enforcement officials said Wednesday.

The drug was encountered in the San Francisco area for the first time six months ago.

In the last two months at least six people in Northern California have died from fentanyl overdoses, according to Dr. Gary Henderson, a pharmacologist at the University of California, Davis. He said test results now pending probably will raise the total to 12.

"It's all over the place in the Bay area," he said. "The overdose cases . . . are just the tip of the iceberg."

Undiluted fentanyl is 7,000 times more powerful than an equal weight of morphine. The drug was developed in the 1950s as general anesthetic. Illicit forms were first reported in 1980 in Southern California street sales, and until recently most sales occurred in that area.

Deaths result because fentanyl is so much stronger than heroin that a slight miscalculation by a dealer or a user can produce an overdose.

OFFICIALS FEAR "ECSTASY" MAY BECOME RECREATIONAL DRUG OF 1980s—"ECSTASY" GAINING POPULARITY IN DALLAS AS CONCERN GROWS OVER ITS SIDE EFFECTS

(By Pat Gordon)

"Ecstasy"—a designer drug flowing into Dallas at the rate of 50,000 to 100,000 doses a month—can leave users with less than the euphoric feeling hyped by its promoters and may even cause brain damage, some medical experts say.

Side effects seen at Parkland Memorial Hospital's emergency room include both high blood pressure, accelerated heart rate, hallucinations and muscle tightening, hospital officials say.

And studies done on Ecstasy's cousin, MDA, show that even small doses can damage cells associated with several basic brain functions.

Even psychiatrists who use Ecstasy in psychotherapy and disagree that it can cause the same damage as MDA believe the latest recreational drug belongs on the controlled substances list.

"It shouldn't be an over-the-counter drug," said Dr. George Greer, a New Mexico psychiatrist who uses Ecstasy in his practice. "It requires medical supervision to be taken safely."

Ecstasy—like other designer drugs—is a legal spinoff of an illegal drug. Underground chemists change the molecular structure of MDA (3,4 methylene dioxy amphetamine), a controlled substance, to produce MDMA (3,4 methylene dioxy methamphetamine), which the Drug Enforcement Administration is attempting to make a controlled substance.

Dr. William Tedford, a Southern Methodist University psychology professor, described Ecstasy as having the same effect as a diluted combination of LSD, cocaine and speed. Like other stimulants and hallucinogens, Ecstasy probably doesn't cause physical addiction, he said.

Officials worry that Ecstasy will become the recreational drug of the 1980s.

"In the 1960s, LSD was the wonder drug," said Ronald Buzzeo, DEA deputy director. "Cocaine was the same for the '70s. I hope Ecstasy doesn't take their place."

Ecstasy first surfaced in 1970 in Chicago. Then—as now—officials believed it was being manufactured in clandestine labs in California. It has since spread from coast to coast, Buzzeo said, hitting the streets in Dallas and other Texas cities in the latter part of 1984.

DEA chemist Frank Sapienza attributes Ecstasy's current popularity to street literature used by distributors that labels the drug a legal euphoric and the use of it by some psychiatrists in their practice.

"That kind of stuff (street literature) is catchy," Sapienza said.

In Dallas, the small white tablets—which sell for $15 to $25 each—are most frequently found in Greenville Avenue bars, at SMU and in North Dallas, said Will Morris, head of the DEA's Dallas division. A 22-year-old SMU student said he sells 500 to 1,000 tablets a week to students and business professionals.

Law enforcement officials in Houston and Austin report widespread use by college students. And DEA officials said that prospective distributors in Beaumont are recruited through parties where they are given samples of Ecstasy, also known as "XTC" and "Adam."

"We're talking about a fad drug," said Tedford, who teaches courses on the behavioral action of drugs. "The largest takers are trendy people—the same ones who patronize the latest restaurants and clothing boutiques."

Last summer, the DEA attempted to put Ecstasy on the most severely restricted portion of the controlled substances list, which would have allowed it to be used only for research purposes. But the agency was flooded by complaints from psychiatrists who said the drug has legitimate clinical uses.

A group of psychiatrists, including Greer, credit Ecstasy with being a mood enhancer that aids psychotherapy. Greer, who has treated 75 patients since 1980 with Ecstasy, described it as a tool that "reduces fear and defenses so people talk more freely."

"For pure MDMA, the dangers are mild compared to cocaine, marijuana and amphetamine," he said. "But no street drug is completely safe because you don't know what you're getting."

Dr. Charles Schuster, director of the Center for Drug Research at the University of Chicago, cautions psychiatrists and street users to "wait and be prudent" until more research has been done on MDMA. He cites studies as showing that rats given MDA suffer degeneration of certain brain cells.

Ecstasy is so closely related chemically to MDA that users could be suffering brain damage that might not show up for years, he said. Both substances, he said, act on cells that are involved with sleep, aggression, sexual behavior and general activity, MDA studies show that activity in those cells remains reduced by 40 percent two weeks after the drug is administered, he said.

"People should know the drug they're taking could have that capability," Schuster said. "I'm more concerned with people on the street taking it in high doses than I am with a single dose given by psychiatrists."

Street literature used to market Ecstasy avoids mentioning side effects but boasts of Ecstasy's ability to bring users peace, happiness, security and freedom.

Street literature also notes that Ecstasy does not produce any particular mood but intensifies the user's present mood. If a person is happy, he becomes elated, the literature claims, and if he is depressed, he becomes severely depressed.

Ecstasy is blamed for having caused two suicides—one in 1978 and a second in 1981, DEA officials said.

"We're just now beginning to see patients here," said Dr. Gray Reed, Parkland emergency room director. "They're expecting a euphoric feeling and as long as they get that they're fine. They come here when they're left with the other (side effects)."

[From the Minneapolis (MN) Star and Tribune, Mar. 14, 1985]

PHANTOM CHEMIST'S SKILL WITH DRUGS HAS FEDERAL LAB AUTHORITIES WORRIED

(By Boyce Rensberger)

WASHINGTON, DC.—A phantom chemist in California is fooling authorities by tinkering with molecules to create legal designer drugs that addicts said are as strong as heroin but that have killed at least 85 people.

"He's clearly a state-of-the-art chemist." said Gray Henderson, a pharmacologist at the University of California at Davis, who coined the term designer drugs. "He'd have to be or he'd kill himself making this stuff. It's that potent."

Drug laws define illegal drugs by their exact molecular structure, so it is possible for the chemist to evade the law by making minor changes in the substance's molecules.

By the time scientists decipher the structure of the chemist's latest product and enforcement agencies take steps to outlaw it—which can consume several months—the phantom chemist simply redesigns the molecule.

The mystery chemist is known to have produced 10 variations of the drug fentanyl, widely used as an anesthetic in surgery but otherwise illegal. Fentanyl has the same effect as heroin, or morphine, and addicts can switch freely back and forth, but it is far stronger than heroin and therefore must be cut to a greater degree for street sales.

Only two of the variations of fentanyl have been outlawed. Pharmaceutical industry researchers have produced an additional 210 variations, none of which ever reached the market, and hundreds more theoretically are possible.

"Whoever this guy is, he's obviously got some chemical training and he's got a good laboratory," said Donald Cooper, a chemist who has analyzed the phantom chemist's products at the U.S. Drug Enforcement Administration's laboratory in suburban Washington. "There are good indications he's cognizant of our legal efforts and he's trying to stay one step ahead of us."

Cooper and other chemists who have been tracking the phantom chemist since 1981, when his products first appeared, have developed a grudging admiration for him.

They cite a drug he made called 3-methyl-fentanyl. It is about 1,000 times stronger than heroin. The amount absorbed through the skin from a smudge on one finger would be "enough to knock you down," said Henderson.

Henderson and Cooper are among the many who believe it is inevitable that designer drugs will spread East. All the deaths so far have been in California except for two in Oregon and one in Arizona.

"If this thing breaks out of the West Coast, we hate to think what could happen," said Ronald Buzzeo, deputy director of the DEA's office of diversion control. "We don't have the legal apparatus to really go after this kind of thing."

[From Time Magazine, Apr. 8, 1985]

SURPRISING CLUE TO PARKINSON'S—A CALIFORNIA STREET DRUG IS LINKED TO THE DISEASE

When George Carillo arrived at the Santa Clara Valley Medical Center in San Jose one steamy July day in 1982, he seemed more a mannequin than a man. The 42-year-old heroin addict was bent over and twisted, drooling and unable to speak; almost every muscle was immobilized. No one knew what to make of his condition, so a call went out for Dr. J. William Langston, the hospital's chief neurologist. Langston took one look and was amazed. Carillo's symptoms suggested that he had been suffering for at least a decade from Parkinson's disease, a nervous system disorder that causes tremors and a gradual loss of mobility. But that hardly seemed plausible: Parkinson's rarely strikes anyone under the age of 50.

Using stiffened fingers to scrawl answers to doctors' questions, Carillo managed to provide a few clues. The symptoms had come on suddenly after he and his girlfriend, Juanita Lopex, 31, had tried a new synthetic heroin. Though the drug had caused an odd burning sensation when injected and hallucinations, they continued to use it for three days; two days later both had frozen into living statues.

With help from colleagues at Stanford University, where he teaches, Langston located Lopez and had her hospitalized. A tip from a neurologist in Watsonville, 30 miles away, led him to two more cases: a pair of brothers, both addicts in their 20s, with advanced Parkinson's symptoms. By now Langston was alarmed. He called a press conference to announce that bad heroin was on the streets; he urged that anyone suffering from stiffness and tremors come forward. The appeal uncovered three more cases.

The seven cases in Santa Clara County attracted the attention of local drug-enforcement officials and Parkinson's researchers at the National Institute of Mental Health (NIMH), who joined the hunt to identify the deadly ingredient in samples of the drug obtained by police. Their task was made easier by an alert toxicologist at the county crime laboratory, who recalled the 1977 case of a Maryland graduate student who had developed Parkinson's symptoms after injecting himself with a home-brewed opiate. The student had been trying to produce MPPP, a substance similar to the pain-killer Demerol, but had accidentally created a related chemical called MPTP. Langston asked Stanford University Chemist Ian Irwin to test the samples for the drug. Sure enough, MPTP was there.

While public health authorities worried about additional cases of drug-induced Parkinson's and police pondered how to stop the sale of a drug that was not illegal *(see box)*, medical researchers could hardly contain their excitement. The tragic outbreak in California could hold the key to understanding and treating Parkinson's disease, which afflicts some 350,000 Americans.

The scientists quickly turned to the task. For years research on Parkinson's disease has been limited by the lack of an animal model on which to test new drugs and treatments. Would MPTP induce Parkinson's in animals? The answer, NIMH Researchers Sanford Markey and R. Stanley Burns soon discovered, was no in rats but yes in monkeys. Says Markey: "That was probably the biggest breakthrough in this story."

The next step was to find out how MPTP did its damage. Doctors have known since the 1930s that Parkinson's occurs as a result of the deterioration of a small, darkly pigmented region of the brain called the *substantia nigra*. This region produces most of the brain's supply of dopamine, a vital chemical in the transmission of nerve signals. Normally, people lose 5% to 8% of the cells in this region each decade of their lives and suffer no serious consequences. But for reasons that are unclear, the loss is more rapid in the case of Parkinson's victims; once approximately 80% of these cells are gone, the symptoms appear. The usual treatment is a drug called L-dopa, which is converted into dopamine in the brain, but the efficacy of the drug may decline after years of use.

MPTP's role soon became clear. Researchers learned that once the chemical enters the bloodstream, it is converted into another molecule (called MPP+) that appears to attack the *substantia nigra* like a guided missile, causing the kind of damage found in all Parkinson's victims. Later experiments showed that if the conversion of MPTP to MPP+ was blocked with chemical inhibitors, a laboratory animal would not develop Parkinsonian symptoms even if given large doses of MPTP. Would human victims also respond to such treatment? At least one drug that blocks MPTP metabolism, Deprenyl, is already used in Europe to treat Parkinson's disease in its final stages. Langston suspects that if used much earlier, "Deprenyl might actually retard the progress of the disease." He has applied for FDA permission to test his theory on Parkinson's victims.

The MPTP cases have led some scientists to suspect that most Parkinson's disease is caused by exposure to toxic substances similar to MPTP. Researchers are looking for culprit chemicals in one rural area of Canada, where the incidence of Parkinson's runs five times higher than in other areas, and on the island of Guam, where, until 1965, one out of five deaths was due to a form of Parkinson's. The United Parkinson Foundation in Chicago meanwhile has mailed questionnaires to 36,000 Parkinson's sufferers around the country, asking them to name every town in which they have ever lived, their drinking-water sources and industries located within a 25-sq.-mi. radius of their homes. Explains Executive Director Judy Rosner: "We want to get a handle on environmental influences."

California public health officials are facing the more immediate problem of what to do about MPTP exposure among addicts. Langston and a team of investigators from the Centers for Diease Control in Atlanta have determined that more than 300 people in the state have used the drug and that it is still being sold on the street. The CDC is now working with state authorities to stem the tide of MPTP and stop it from spreading beyond California.

But no one knows what will become of those already exposed. Of 150 MPTP users examined by CDC researchers, as many as half had subtle signs of Parkinson's. Says Langston: "There may be a large number of people out there with half the nerve cells they're supposed to have." In ten or 15 years, he predicts, as these addicts continue to lose *substantia nigra* cells as part of the normal aging process, California may become the scene of a Parkinson's epidemic.

[From the New York Daily News, Mar. 17, 1985]

SYNTHETIC HEROIN, REAL THREAT

(By Arthur Browne)

New superstrains of synthetic heroin—most of them legal—have surfaced in New York and triggered fears that the often-deadly, laboratory produced narcotics will replace the far less powerful, traditional heroin now flooding the city's illicit drug market.

The drugs, which can be 3,000 times more powerful than heroin, present a lethal threat to addicts and often confound police because detection is extremely difficult.

Because most of the drugs, produced in clandestine chemical labs, are potent, inexpensive to make and legal, officials fear that synthetic heroin could revolutionize narcotics use and trafficking in the United States.

The synthetics, described by experts as the "drugs of the future," have been formulated from newly developed chemical compounds. Most can be sold, possessed and consumed without penalty because they never have been outlawed by the federal government.

Widely distributed in some areas of California—by some estimates 20% of that state's addicts now use synthetic heroin—the new drugs surfaced here last July when a sample of one was purchased in a federal Drug Enforcement Administration undercover investigation in Brooklyn.

Because of the growing popularity of the synthetics in California, experts believe that their use will increase markedly nationwide. Some predict that the clandestine laboratories producing them will eventually replace the poppy fields of Asia as the primary source of heavy narcotics in America.

According to the experts, the appeal of synthetic heroin over the traditional drug is clear:

A small laboratory equipped with basic scientific equipment can produce enough synthetic heroin in just a few weeks to supply the addict population of New York City, if not the country, for years. The cost to produce it: no more than $10,000.

Some forms of the drug are as much as 3,000 times more powerful than traditional heroin—a potency that only requires microscopic dosage levels. Tens of millions of doses can be stored easily in a container on a closet shelf or in a desk drawer.

Like traditional heroin, the synthetic variety is mixed with cutting material, such as lactose, before it is sold, but its minute presence in the mix can be chemically detected only through sophisticated scientific tests. Most law enforcement laboratories—including the New York City police lab—rarely conduct such tests.

The drug cannot be detected by routine blood and urine tests, thus making it an ideal substance for prison inmates, parolees, professional athletes and others who may be subjected to drug testing.

With two exceptions, synthetic heroin is legal.

"What we're talking about is the drug of the future," said Robert Roberton, chief of the California Division of Drug Programs. "It will replace heroin. Why bother to go through the cops and robbers? Why bother with growing and refining and smuggling heroin over the borders when you can make something just as good, if not better, so cheaply and quickly?"

"I think the Mafia is probably more worried about this than the government is," said Gary Henderson, an associate professor of pharmacology at the University of California at Davis who has studied synthetic heroin extensively.

The development of synthetic heroin is the latest outgrowth of a trend dubbed "designer drugs." These are substances—such as high quality LSD, methaqualone (Quaalude), speed and PCP, the active ingredient in angel dust—that are being formulated in clandestine labs to suit various tests in drugs.

"Chemists out there are experimenting in laboratories, attempting to make drugs to suit different tastes," said Roberton. "People can say, 'I want a drug that keeps me high for three hours. I want to feel a certain way. I want to go back to work without a hangover.' I think we have the technology and are moving in that direction."

Chemically, the various available forms of synthetic heroin are all derivatives of a drug called fentanyl, a legitimate and widely used surgical anesthetic. As used in hospitals, fentanyl is about 20 times as powerful as heroin, but its effects last only a half hour or so.

By altering fentanyl's molecular structure, however, chemists can create new compounds—or analogues—of the drug that are much more powerful and long lasting. And, although they are far different chemically from traditional heroin, the analogues react in the body just as heroin does, producing the same high and the same addiction.

Seven analogues of fentanyl have been developed so far. They range from a compound called alpha-methyl fentanyl, which is estimated to be about 50 times stronger than heroin, to 3-methyl fentanyl, the substance believed to be as much as 3,000 times stronger. They can be produced in standard college chemical laboratories, Henderson said, but the more powerful the analogue the more sophisticated the chemist must be.

The first fentanyl analogue surfaced in California in 1979 under the street name of China White. It made its way here the same year and was sold in Harlem under the same name. It did not catch on, however, apparently because in its early versions addicts found the drug difficult to dissolve and inject. Over the next few years, there were sporadic reports among addicts that it was being sold again, but such claims were never officially confirmed.

In California, the synthetics grew steadily in popularity. Their presence drew official attention when eight addicts died of overdoses in Orange County, which is south of Los Angeles. Their deaths were initially attributed to heroin, but autopsies showed no trace of drugs. Standard tests on narcotics found in their clothing or near their bodies also produced the same result: The white powder they had injected appeared to be heroin, but was not. In fact, the tests suggested it was just harmless lactose and other cutting materials.

Samples of the narcotics were then sent to Henderson. Using sophisticated testing equipment, he identified them as containing tiny amounts of alpha-methyl fentanyl, the first known fentanyl analogue. Since the compound had never been seen before, it had never been placed on the DEA's list of unlawful substances. The drug was therefore legal.

When it became clear that alpha-methyl fentanyl was being widely abused, the DEA placed it on its schedule of illegal drugs. The illicit labs responded by creating new fentanyl analogues with slightly different molecular structures. Because these new analogues were compounds that had never been specifically outlawed, they too were legal.

Since then, Henderson has identified seven fentanyl analogues, and he estimates that chemists can produce hundreds more. Of the seven, only alpha-methyl fentanyl and the super potent 3-methyl fentanyl have been outlawed. The DEA is currently moving to add three others to its list of proscribed substances.

"There could be hundreds of fentanyl analogues," said Ron Buzzeo, deputy director of the DEA Office of Diversion Control in Washington. "You get a good sharp chemist and he can play with the structures and develop any analogue he wants. That way he can stay one step ahead of us."

According to Roberton, fentanyl analogues are now responsible for 89 deaths in California, with the number growing by about two a month. The most potent and dangerous of the analogues is 3-methyl fentanyl, which the DEA outlawed on an emergency basis last year.

Because it is approximately 3,000 times stronger than heroin, according to Henderson, a user needs a dose measuring less than one microgram—a millionth of a gram—to stay high for between four and six hours. By comparison, it would take 300,000 such doses to make a tablet the size of a common aspirin.

"An active dose is just about the smallest amount that you can see without a magnifying glass or a microscope," said Henderson. "Anything even slightly larger than that is likely to be fatal."

The tiny dosage size makes the drug both difficult to administer safely and hard to detect chemically when it is mixed with even a small quantity of cutting material for injection. The sample of snythetic heroin purchased by a DEA undercover agent in Brooklyn last July, for example, is believed to have contained 3-methyl fentanyl, but the DEA is not certain.

"We got in a small sample of suspected heroin," said Jeffrey Weber, supervisory chemist of the DEA's northeast regional lab in New York City. "The chemist analyzed it. It obviously wasn't heroin and we found it contained a fentanyl analogue, most likely the 3-methyl analogue. But since the sample was so small, we couldn't absolutely confirm it."

Law enforcement officials are at a loss to estimate how much synthetic heroin is on sale in the city's drug supermarkets. The Police Department, for example, has never recorded a seizure of the drug, but the department's crime lab concedes that may be because it does not routinely conduct the rigorous kind of testing needed to detect and identify the new forms of synthetic heroin.

"Basically we have never seen them," said Howard Harris, director of the lab. "But we might have missed them if they came in. If we simply tested a bag of drugs for heroin, we wouldn't find them. If that happened, we might classify what we found as a 'beat bag' that contained no drugs at all."

[From the Santa Ana (CA) Orange County Register, Apr. 23, 1985]

SYNTHETIC PAINKILLER SOLD AS HEROIN KILLS 90 STATEWIDE, 10 IN COUNTY

WASHINGTON.—A powerful synthetic painkiller being sold throughout California as high-quality "China White" heroin has killed 90 people in the state, 10 of them in Orange County.

And until today, the newest and deadliest variety of the synthetic drug was perfectly legal.

The Drug Enforcement Administration today exercised new emergency powers and outlawed a synthetic heroin so new that it hadn't been listed as a restricted drug.

"What normally would take us six to 12 months, we can now make illegal with a stroke of a pen." said Ronald Buzzeo, deputy director of the DEA's diversion control program in Washington. "The new law helps us a lot: it give us the power to prosecute."

Authorities say expediency is crucial in the battle against a new generation of chemically synthesized heroin substitutes nicknamed "designer drugs."

Federal and state laws define illegal drugs by their exact molecular structure. Thus, a renegade chemist may evade the law by tinkering with the molecules to design new drugs not yet banned.

And until now, DEA officials stay agents have lagged hopelessly behind the chemist, believed to be operating out of a clandestine laboratory somewhere in California where he has been cooking up designer drugs that produce the same potentially deadly euphoria.

The Orange County Sheriff Coroner's Office was the first to encounter the designer drug in California. Three days after Christmas 1979, police found two Anaheim men in their 30s lying dead near heroin paraphernalia and samples of a white powder.

Local tests couldn't identify any illegal substance. Thirteen more users, including eight in Orange County, died before the substance was isolated in 1981 by forensic chemist Donald Cooper at the DEA's laboratory outside Washington.

Cooper discovered the mysterious powder was a designer version of fentanyl, an anesthetic widely used during major surgery.

Called alpha-methyl fentanyl, it is also many times more powerful than heroin.

By the time the DEA moved to ban the new drug—a process that took many months—the underground chemist had come up with a new version. When DEA outlawed the second modified drug, a third one popped up, officials said.

Last year, Rep. Dan Lungren, R-Long Beach and west Orange County, helped push President Reagan's omnibus crime package through Congress. One section gave the DEA emergency powers to speed up the banning process dramatically.

"It is nice to have something in place now that can react to these problems as they arise," Lungren said.

Although narcotics officers can now quickly outlaw new drug variants, also know as analogs, they aren't any closer to catching the phantom chemist.

"The law may ease the frustration of law enforcement, but he'll just come up with another analog," said Gary Henderson, a pharmacology professor at the University of California at Davis, who coined the term designer drugs."

"Obviously, a state-of-the-art chemist is doing it." Henderson said. He said he believs the work is too ingenious to be anything but the work of one person.

The chemist will be able to say one step ahead of the DEA bans by dreaming up new versions until, Henderson said, "the restricted drug list will look like the New York telephone book."

Henderson and other chemists tracking the work of the phantom chemist since 1979 have developed a begrudging admiration for him. "It is like somebody who is operating on the dark side of the Force," he said. "You admire his skill, but not what he is doing with his ability."

Drug authorities say the chemist, or anyone else who gets involved, could make enough of the designer drug in a few weeks to supply the nation's heroin habit for years.

To test its new emergency powers, the DEA chose to outlaw the chemist's sixth, and most potent, version of fentanyl. This chemical cousin, 3-methyl fentanyl, is 1,000 times more powerful than heroin and nearly as many times as deadly.

One dose of 3-methyl fentanyl, passed off by pushers as a pure grade of the Asian heroin China White, would contain only about two micrograms, or two millionths of a gram of the drug, chemists say. The rest of the "fix" is lactos.

"This (drug) frightens us because the drug is so extremely potent." said Robert Cravey, chief toxicologist in Orange County's Sheriff-Coroner Office, who has been following China White varieties for six years.

Orange County has not seen any China White deaths since the original 10 in 1979 and 1980, Cravey said. Last year's 48 overdoses and the 16 heroin deaths this year have been from naturally derived drugs.

Synthetic China White has been linked to at least 90 deaths in California since 1980, with 50 of them last year, said Robert J. Roberton, chief of California's Division of Drugs in Sacramento.

Some of the addicts were "found with the needle still in their arms," he said.

Henderson, who has tracked all the China White deaths, said the overdoses only reflect a small fraction of those using the drug. Novice users are the ones dying, he said.

More experienced addicts know more about how to measure a nonlethal dose.

"We figure that 18 percent to 20 percent of (the estimated 125,000) heroin addicts in California are using the fentanyl," Roberton said. Some are beginning to ask for it by name.

"It is not a big-city, ghetto-type drug," Henderson said. Designer drug users are more often middle class, white and better educated than downtown addicts, he said.

So far, use of synthetic China White is spread around California, but has not gone beyond its borders.

It is only a matter of time, drug authorities say, until other laboratories and organized crime move into the lucrative business.

Law enforcement authorities haven't gotten any closer to catching the phantom chemist since the designer drugs hit the streets, Henderson said.

THE CASE OF THE FROZEN ADDICT—IT STARTED AS A MEDICAL MYSTERY IN SAN JOSE—AND IT MAY END UP SOLVING THE RIDDLE OF PARKINSON'S DISEASE

(By Larry Thompson)

Dr. Phil Ballard jabbed a sharp instrument into the tender arch of a 42-year-old drug addict's foot, but the man didn't flinch. He just lay on the county hospital bed drooling.

The psychiatrists had asked Ballard and his boss, Dr. J. William Langston, chief of neurology at the Santa Clara Valley Medical Center in San Jose, to look at the drug addict. The psychiatrists thought his stupor might be catatonic schizophrenia—but something about that diagnosis just didn't seem right.

Ballard jabbed the addict's foot to see if his brain was still connected to the nerves in his feet. Intact nerves always jerk the foot away, even if the subject is catatonic. The addict remained motionless. But his mind, trapped in a frozen body, screamed in pain.

"He was like a pillar of salt," Langston recalls. The man couldn't stand, couldn't speak and couldn't help them help him.

Then Ballard noticed that the addict could move his fingertips. Slipping a pen between the man's fingers, Ballard asked him his name. "George Carrillo," he wrote in a halting script. "I'm not sure why or what is happening. I can't move right. I know what to do. It just won't come out right."

"This was stunning," says Langston, a bearded 40-year-old physician who teaches neurology at Stanford University. "Here's this pillar of salt, and this was the first clue that he was completely normal inside."

George Carrillo was also the first clue that a kitchen chemist making illicit drugs in Santa Clara County had cooked up a bad batch of a Demerol look-alike. Instead of euphoria, at least seven Bay Area drug users had bought fixes of brain damage that left them paralyzed.

And Carrillo was the first clue in a medical detective story that would change Langston's life, propel him into national prominence as a brain researcher and start him on a research project that someday could change the treatment of Parkinson's disease.

But on that June afternoon in the VMC neural behavioral unit, Bill Langston knew only that he had a heroin user named George Carrillo who couldn't move.

The two doctors checked for a variety of drugs that can cause such reactions. Nothing. They briefly considered carbon monoxide poisoning and a rare form of copper poisoning called Wilson's disease. Again nothing. Carrillo's body remained frozen. Whatever is was, it wasn't wearing off.

"We kept hearing that his girlfriend had something very similar. About a week later, we got her to come in," Langston says. "To me it was just amazing when I walked in and saw her."

Juanita Lopez, 31, sat motionless, no expression on her face; her reptilian eyes seldom blinked. "I have since learned that look," Langston says. "They all have it."

Langston found out that Carrillo and Lopez had had four bindles of a new synthetic heroin. (A bindle is a small piece of paper folded to hold about a gram of the drug.) They had bought the packets from a Mountain View drug dealer early in the summer of 1982. The stuff had just hit the street. When Carrillo used it, Lopez said, he immediately began hallucinating—something that never happened with real heroin. And the new stuff burned when shot into a vein. They injected three of the four bindles anyway.

On July 4, Lopez awoke to find she couldn't get out of bed. Carrillo too felt stiff. Neither knew the cause.

Four days later, Carrillo was jailed, in part because the cops thought the stiffness they saw in him during a hearing was caused by PCP, a drug known as angel dust on the street.

While in jail, Carrillo got worse. Swallowing became harder, movement impossible. Guards took him to the county hospital emergency room. Doctors there gave him an antidote to counteract a common type of drug reaction. Then they sent him back to jail. But Carrillo got worse, and ended up being admitted to VMC.

He had the classic symptoms of Parkinson's disease—a mysterious, debilitating illness that strikes mainly older people (one in 100 over the age of 60).

Carrillo's expressionless face, like Lopez's, stared straight ahead. If Langston stood him up, Carrillo could shuffle unsteadily forward, but he stooped like a man off balance, trying to catch up with his leaning upper body so he wouldn't fall on his face.

"He moved like a block of wood," Langston says, "I could not tell him from a Parkinson's patient." Parkinson's patients suffer whole-body rigidity. To turn their heads to see something, they must turn their entire bodies—when they can move at all.

Lopez had the same symptoms, and she also shook like a person with Parkinson's disease. But the cause remained a mystery.

After some negotiating, Langston persuaded Lopez's sister to bring in the remaining bindle of synthetic heroin—a critical first sample of the drug that held all the answers.

Chemical analysis showed that it contained a drug from the merperidine family, which includes familiar drugs like the painkiller Demerol, but the test didn't show which one. The bindle also contained some related chemicals that produced a peculiar, and unrecognizable, pattern on the test printouts.

Since the chemicals in the sample remained unidentified, they couldn't explain the paralysis. Langston and company needed a break if they were going to find the answer.

Phil Ballard needed a break, too. He had been at VMC for the past year completing his training in neurology. An old friend invited him to a dinner party in Santa Cruz that weekend. There he met Dr. James W. Tetrud, a neurologist who practices in Watsonville and Santa Cruz.

As doctors do at parties, they talked about their unusual cases. Tetrud told Ballard about a patient he had in Watsonville who was frozen stiff. He had never seen anything like it before. And his patient was supposed to have a brother with the same problem.

Struck by the apparent similarities, Ballard decided to stay over and see Tetrud's Watsonville patient. The man was a dead ringer for Carrillo and Lopez. He had injected a new synthetic heroin over several days and then had frozen up. So had his brother. They had lain frozen in their apartment for days. If their mother hadn't come by to check on them, they would have died there.

"If Ballard hadn't gone down to dinner that night, we would not have had any idea of the scope of the problem and we would still be playing around with that one sample," Langston says.

They now knew that there was some bad dope on the street, and they decided to warn the public about it. The hospital arranged a press conference and the news reports brought in a 30-year-old woman. Her boyfriend had been damaged, too, but not badly. Another man and another woman were identified later.

All had injected the new synthetic heroin. All had frozen up to some degree. Most had been in other hospitals where doctors misdiagnosed their problem as catatonic schizophrenia.

Langston now had seven paralyzed patients and no answers. He still didn't know which chemical caused the paralysis, or what part of the body was damaged, but he was sure it was related to Parkinson's disease. The similarity of the symptoms was too compelling.

Most of the patients had the classic upper-body quivers of Parkinson's disease. Every second, their hands and arms shook with three to four tremors. Typically, the first two fingers and thumb rubbed in opposition, like a pharmacist rolling fresh pills. Their muscles became stiff. Instead of moving fluidly like a skater on ice, the muscles behaved like cogs in a machine, lurching forward as though ratcheted.

One woman had a sort of rigidity of the eyelids. She could blink reflexively, but when she closed her eyes voluntarily, it would take several minutes of struggling before she could get them open again.

Lanston had held off giving any drugs to Carrillo and Lopez because he didn't know what was going on. After a week and a half, with so many similarities to Parkinson's disease showing up, he gave them L-dopa, the same drug used to treat Parkinson's.

"It was like melting an ice block," Langston says, shaking his head. "It was like bringing a statue to life."

In just a few days, the patients had near normal movement. "Without that chemical in your brain," Langston says, "you don't function."

"That chemical"—dopamine, a small molecule produced in the brain stem from L-dopa—acts like an essential lubricant between the thought of lifting a finger and the actual movement. Parkinson's patients, like Langston's drug abusers, don't have enough dopamine in their brains. Without it, commands that once raced from the brain to the muscles stop, and conscious movement stops, too.

But suspecting that something in the fake heroin was causing the Parkinson's-like disease in the drug abusers was not the same as knowing what it was or how it did the damage.

Langston still needed answers. First he got more drug samples, essential clues to piecing together the mystery. Watsonville police raided the home of Tetrud's patient and found six to eight bindles of the synthetic heroin. Langston farmed out samples to whomever he thought could help.

Some of the powder found its way into the hands of Halle Weingarten, a forensic toxicologist at the crime lab of Santa Clara County. Weingarten suspected PCP, but she didn't find any in the sample. She could say that it looked like a drug from the merperidine family, which Langston knew, but that was all. "I was stymied," Weingarten says.

Around the same time, Jim Norris, a criminalist in the same crime lab as Weingarten, was asked to decipher a packing list of chemicals that had been given to police by a tipster. The chemicals on the list had been delivered to what county narcotics agents believed was a clandestine laboratory for making illicit drugs.

The list was puzzling: 50 gallons of ether, 40 gallons of acetone, 100 pounds of lithium metal (a catalyst), 88 pounds of bromobenzene, 220 pounds of propionic anhydride, and 44 pounds of 1-methyl-4-piperidone. Altogether, Norris estimated, the raw materials were worth about $10,000, and all were legal.

But what could someone make with them?

Norris pondered the list of chemicals and figured out that it included all the ingredients for making the merperidines Weingarten had found in her sample. The lab that the narcotics people had been investigating, he surmised, probably had made the paralyzing drug.

Deputy Sheriff Dave Weidler, a giant of a man with blue eyes and fading golden hair, was the agent on the countywide narcotics task force who got the case. He wanted to get the lab so badly he could taste it.

But Weidler was stuck. Fearing retribution, the tipster who had turned in the list of chemicals wouldn't provide the testimony Weidler needed to get a search warrant. Without probable cause that a crime had been committed, Weidler couldn't even get a judge's attention. So he and Assistant District Attorney Doug Southard decided to do a little creative legalizing.

The clandestine lab was filled with volatile, flammable solvents. Clearly, they reasoned, those solvents were a fire hazard, so they convinced fire officials to conduct a surprise public safety inspection. Weidler went along.

The man who answered the door was calm, intelligent, clean-cut and very cooperative, Weidler recalls. The chemist, whom Weidler would not identify, told the investigators that he was "experimenting to develop Sno-cone flavors and moisturizing creams." But to Weidler's practiced eye, the place "had the appearance of a typical dope lab."

The chemist wasn't cooking that day. The glassware, though set up, was clean. Weidler had brought along a field presumptive test that can be used to identify classes of common illegal drugs like angel dust, heroin or speed.

"If we had gotten one of those to turn positive, we would have frozen the place and gotten a search warrant," Weidler says. But nothing turned up. The kit didn't include a test for merperidine look-alikes. Weidler was powerless. All he could do was take samples back to the crime lab.

The law controls some drugs in the merperidine family, like Demerol, but it does not control them all. When Weidler analyzed the samples, he found drugs that violated the spirit of the law. But, because they didn't violate the letter, it wasn't illegal to make, possess or inject them. The chemist was untouchable.

Fire officials gave him a day to get rid of the hazardous solvents, and that was all they could do. A repeat inspection found the lab cleaned up. Although he may have damaged the brains of hundreds of Bay Area drug users, the chemist remains safely beyond the law.

Back at VMC, Langston was still trying to figure out which of the chemicals made in the clandestine lab caused the paralysis.

The next break came on a Saturday morning as Halle Weingarten idly sipped coffee over the morning paper. Suddenly, she says, "It just clicked. I remembered reading an article a year or two before that."

The article, published in the inaugural issue of an obscure journal called *Psychiatry Research*, described a 23-year-old graduate student who had developed the paralysis of Parkinson's disease after injecting his own homemade merperidine look-alikes.

"That was a fluke basically," Weingarten says. "A friend of the director of this lab had given him a copy of the journal to look at. He had seen that article and showed it to me because he thought it was very interesting, and then we both put it out of our minds."

The article fascinated the two forensic toxicologists, because few drugs cause Parkinson's-like symptoms.

In many ways, Parkinson's disease remains as mysterious a neurologic disorder as it was when English physician James Parkinson first described it in his 1817 phamplet, *Essay on the Shaking Palsy*. It took more than 150 years before researchers at the University of Vienna figured out that people with Parkinson's didn't produce as much dopamine as normal people. The cells that produce dopamine—a small patch of black-stained brain cells called the substantia nigra—die off, and the resulting shortage of the chemical inhibits the passage of nerve signals between nerve cells.

Although dopamine is produced by nigral cells at the base of the brain, the target cells are much higher up in the brain, in the striatum, where the origins of voluntary movement lie. If the nigra stops producing sufficient quantities of dopamine, the unstimulated striatum slows movement, makes muscles stiff and eventually, in the most severe cases, brings paralysis.

When doctors discovered the dopamine shortage in Parkinson's patients, they figured that simply replacing the missing dopamine would solve the problem. But dopamine itself will not enter the brain, so doctors now use its metabolic precursor, a chemical called L-dopa, which the brain chemically changes into dopamine.

It appears that the nigra stops producing dopamine because the dopamine-producing cells die off for unknown reasons. L-dopa helps because the remaining nigra cells work overtime to convert it into dopamine. As Langston explains, however, this is a losing situation. As the disease progresses, the doctor has to flood the brain with larger and larger doses of L-dopa, and eventually the high doses themselves become poisonous.

How or why the nigral cells die in Parkinson's disease remains a mystery. For the graduate student, however, the cause was quite clear.

He had started making his own drugs, including MPPP, a substance that produces a heroin-like high, but causes no brain damage. Then he took some short cuts: increasing the heat of the reactions, decreasing the reaction time. The short cuts proved nearly lethal; instead of producing MPPP, he made MPTP, a chemical cousin of the first drug. MPTP, it turned out, destroys nigral cells more selectively than an Exocet missile can down a MiG 25.

In November of 1976, according to the article that Weingarten had remembered, after injecting this "sloppy batch" for several days, the graduate student "developed a state of numbness, severe rigidity, weakness, tremor, flat facial expression and altered sensorium." A neurologist concluded the graduate student had Parkinson's disease, and gave him L-dopa. The drug restored normal movement to the 23-year-old, but he died of an illicit drug overdose two years later.

The case had created a lot of excitement among experts at the National Institute of Mental Health, a federal research center where the student had been treated. If they could figure out which chemical in that sloppy batch had caused the Parkinson's-like symptoms, then they might be able to use the chemical to create an animal model for Parkinson's disease—one that would allow them to test possible treatments they could not test on human patients. The absence of such a model had hampered research for years.

But the NIMH researchers couldn't figure out which of the chemicals in the sloppy batch had caused the brain damage. They repeated his synthesis, and injected the various components into test animals. None of the chemicals produced Parkinson's disease.

Interested dwindled. With the chemical unidentified, the report became tentative, publishable only in a minor journal. But Weingarten remembered it—and for the VMC investigators, that was the last key link.

"When I got the article and read the case report," Langston recalled, "it was virtually electrifying. Here were our patients just verbatim. At this point, I was already convinced that this guy had done the same thing to himself that our patients had done."

But a key problem remained: Which chemical in the sloppy batch of heroin caused the brain damage? NIMH researchers never did figure it out. They had done exhaustive chemical analysis and identified every compound in the graduate student's dope, but none of the compounds caused the brain damage in lab animals.

Langston had sent a sample of the locally produced drug to Ian Erwin, then working in the drug assay lab at Stanford University, now a part of Langston's research team. Erwin had run some tests, but he too had been unable to identify the chemicals.

After reading the NIMH paper, Langston called Erwin and read the formulas over the phone. By matching the atomic weights in the NIMH paper with the analysis he'd done on the locally produced drug, Erwin predicted that a chemical called 1-methyl-4-phenyl-1,2,5,6-tetrahydropyridine (MPTP) had caused the brain damage.

Langston called the NIMH group in Bethesda and talked to Dr. Stanford P. Markey, the group's chemist. "'It says here in your article that you tested animals. Were you able to reproduce it in the animals?'" Langston recalls asking. "He said, 'No, we were able to produce catatonia, but just about anything does that in rats.'

"I asked, 'Did you try the MPTP, the byproduct?'" Excitement grows in his voice as he retells the story. "There was a silence. And he said, 'You know, it's the only one we didn't try.'

"And I remember that moment because I realized that we had it," Langston says. He likens his excitement at the moment of discovery to that of "an explorer who steps somewhere no one has ever stepped before, seeing something for the first time. You know it's not going to last very long, but you're the first there, and it's just a kind of exhilarating feeling."

By comparing two samples of MPTP to the local samples, Langston's group proved that the chemical was present in the synthetic heroin. Langston spent months ironing out details of the investigation, but now they were sure: MPTP was the chemical that caused the Parkinson's symptoms.

After Langston's group figured out which chemical caused the brain damage, NIMH started testing it in monkeys. The symptoms produced in the monkeys further confirmed that this one chemical caused the brain damage.

The NIMH researchers still had half of the brain from their original patient. they sent the slides to Langston, who reviewed them with Dr. Lysia Forno, a neuropathologist at Stanford and an expert in the neurological changes caused by Parkinson's disease.

The graduate student's brain showed that MPTP destroys the dopamine-producing cells in the brain of a drug user, just as Parkinson's disease does in the brains of the elderly. Because other areas of the brain also are affected by Parkinson's "no one has ever been sure how many of the symptoms come just from the substantia nigra," Langston says. "This is the first time that we ever had good evidence that probably most, if not all, of the clinical manifestations of the disease relate to the nigral changes and not to these other areas.

"Had we not been able to identify it," Langston adds, "I can tell you that the interest in it would have dwindled off. You work real hard when something first hits, and then after you run into a brick wall after a while you finally get less and less interested and it dies, just like it died back there at NIMH."

But the connection was now absolute. With this powerful new tool for studying Parkinson's disease at hand, Langston began trying to raise enough funds through government and foundation grants and private donations to set up a major Parkinson's research center at Valley Medical Center. Already, he has received a $150,000 grant from the Retirement Research Foundation in Chicago. It's the first of what could become a three-year grant to carry on the basic research. And he has started putting together a team of researchers that will work out of the Institute for Medical Research, which has a research building next to the VMC. The team will be using MPTP to create Parkinson's disease in animals so its cause and progress can be studied in the brain.

Langston was able to get two Stanford University medical students to spend the summer looking for other drug users who might have used the bad synthetic heroin. The students turned up dozens of people from King City to Oakland who probably had been exposed to the contaminated drug. Some had moderate damage, others only minor symptoms.

"I think the total number is going to be 150 people," Langston says. He fears that at some point there will be an epidemic of Parkinson's disease among these drug users who may not be damaged badly enough to cause paralysis, but whose dopamine-producing cells are disappearing fast.

And for the patients he has already, the future is not bright. "Four of the patients will die, without (dopamine)," Langston says. They will freeze up and eventually die from malnutrition or infection.

Like real Parkinson's victims, Langston's young patients are getting worse. the range in the dose of L-dopa that he can give to some of the patients is getting smaller. Below one level, they freeze; above another level, L-dopa itself causes bad reactions. George Carrillo, for example, hallucinates when his L-dopa dose is too high. Juanita Lopez shakes uncontrollably when her dose is not finely tuned.

But while things seem grim for the people already damaged by the drug, the promise for all of the estimated 1.5 million Parkinson's patients is bright.

The first epoch of basic research in Parkinson's disease led to the discovery of L-dopa's ability to free Parkinson's patients from their paralysis. Langston's discovery seems to have opened the second epoch, a rush of basic research into the way Parkinson's disease destroys the brain and the body's ability to move.

"Even in our lab, it has given us second life after years and years of not finding anything," says Dr. Andre Barbau, chairman of the department of neurology at the University of Montreal, and the first doctor to use L-dopa on patients. "We did find something important (L-dopa), but that was early. Dopa was so successful that people abandoned research on the cause of the disease in the last 20 years. They were all competing to find a better dopa."

After it became apparent that better forms of L-dopa would not be easy to find, Barbau returned to working on the basic problems of Parkinson's disease. But "in the last couple of years," he says, "we have been turning around in circles."

Now researchers have begun using the Langston's breakthrough discovery to probe the molecular and cellular details of the disease. In October, the world's leading Parkinson's researchers met in Montebello, Quebec. many of the excited researchers gave reports based on the use of Langston's drug.

And though Langston himself is reluctant to state it so strongly, it seems clear that the discovery of MPTP and its ability to cause Parkinson's disease in animals is likely to produce the clues needed to prevent—or maybe one day, even treat—this mystifying illness.

[From the Detroit News, June 13, 1985]

THE DESIGNER DRUG MARKET: AMERICA HAS LOST THE WAR

(By Jack Shafer)

The seeds of a new criminal enterprise were shown in the early 1960s when a group of chemists tinkering in California basement laboratories discovered a way to turn industrial chemicals into gold. Like the boys from Apple who set IBM and the rest of the computer world on its ear with a computer assembled in a garage, the basement chemists revolutionized the drug market with drugs they synthesized in their clandestine laboratories.

Some of the drugs, such as LSD and PCP, are well-known. Others, like methamphetamine and methaqualone, are better known by their street names, "speed" and "ludes." Most people haven't yet heard of the more esoteric products of clandestine labs, like MDMA and syntethic heroin-substitutes. But that's about to change. Heroin, cocaine, and marijuana are as obsolete as horse and buggy. The drugs of the future have arrived, and they are made in test tubes.

Over the last 20 years the illicit synthetic drug trade has transformed itself from amateur-hour status into a 10 billion a year industry run by aggressive lone-wolf chemists, motorcycle gangs, and segments of the Philadelphia mob. This new criminal enterprise has already become as entrenched as loan sharking, the numbers, and prostitution. Underground labs synthesizing hallucinogens, stimulants, and sedatives can be found in Detroit and almost every major city in the nation.

Clandestine labs may have originated in California but they are no fad. They have sparked a permanent shift in the market for drugs that may eventually put the heroin warlords of Burma and cocaine cowboys of Colombia out of business. At the same time they threaten to flood the country with an unstoppable wave of drugs of abuse and render the current drug laws unenforceable, once and for all.

Consider for a moment the economic advantages that synthetic drugs offer to a drug dealer. A chemist can turn a few hundred dollars of industrial chemicals into PCP or methamphetamine worth millions of dollars on the street. The effects of almost every traditional drug can be simulated by a synthetic. The dealer can spare himself the hasle of customs inspection, or the chance of being detected by U.S. Navy destroyers that now patrol the Caribbean on the lookout for smugglers. By eliminating the risks of drug smuggling and reducing the size of the distribution network, the purveyors of synthetics can pull in fantastically higher profits.

The advantages go on and on. The formulas for these drugs can be found in libraries or purchased on the black market, making it possible for anyone to enter the market. Many of the chemicals needed to make the drugs are easily purchased from the chemical supply houses. The chemicals that are monitored by the police can be acquired on the black market.

Recently the market has taken a high-tech turn as sophisticated chemists have devised "designer drugs" that closely mimic the effects of heroin. LSD, and PCP. The designer drugs, however, have another designer wrinkle. They are designed to be completely legal. Legal drugs? It sounds like a drug dealers' paradise, but it's true. Because state and federal drug laws ban drugs by their specific names, all it takes to turn an illegal drug into a legal one is a subtle rearrangement of its molecular layout. If the new compound is not on the state or federal list of prohibited drugs the manufacture and use of it violate no law.

Legal "designer versions" of PCP, the hallucinogens, Quaalude, and methamphetamine routinely turn up on the market. And in California, where the clandestine drug lab trend started, chemists are now making synthetic heroin-substitutes that perfectly mimic heroin. These analogs or chemical cousins of fentanyl, a legitimate synthetic narcotic used in surgery, give heroin users the same euphoria that heroin does, and works like heroin to stave off withdrawal. Like heroin they are also very addictive. There is, however, one problem with these legal high-tech highs. They kill. According to Dr. Gary Henderson, a pharmacologist at the University of California at Davis, the clandestine fentanyls have killed off 85 users on the West Coast since 1979 and continue to kill at the rate of two a month.

It takes, at the least, a couple of months to outlaw a designer drug. The first "designer heroin," alphamethyl fentanyl, was banned eight months after it was detected, but since then the clandestine chemists have spun off a half-dozen new and legal versions of it. Because nature has provided the chemical patterns for millions of potential synthetic drugs of abuse, chemists can devise new ones each time the government bans the last one.

Even if the government found a way to ban designer drugs before they appeared, clandestine labs would still be an unstoppable source of drugs. Each year 200 clandestine labs are seized by the police, but by the government's own estimate, some 800 labs go undetected. One lab can put millions of doses on the market in a week, making it impossible for police to stem the synthetic tide. The history of PCP proves the point. After 15 years of concentrated law enforcement effort and escalating criminal penalties, which punish repeat offenders with 40 years in jail and $500,000 in fines, PCP remains one of the easiest and cheapest drugs to buy on the street.

The inescapable conclusion to be drawn from the synthetic drug revolutions is that the war on drugs is over. The government has lost. The technology to make drugs of abuse is just too widely dispersed and too simple to replicate for the government to stamp out.

No serious observer of drug policy expects the government to surrender. Instead, new tougher drug laws will be passed by legislators. But these sanctions, which have never worked against traditional drugs, will be even less effective against the synthetics. These drugs are an inevitable part of our technological evolution. Sooner or later—after spending billions more tax dollars on the increasingly futile "war against drugs"—we will have to come to grips with that truth and reshape our drug laws. Adults who insist on taking drugs should have access to the safest ones science can make.

THE INTELLECTUAL'S HEROIN

As local drug counselors battle the rise of heroin use and its dangerous imitator, MPTP, a new drug is making its debut in Sacramento.

Fentanyl is widely used as a painkiller in hospital operating rooms and has made its way to the streets as a substitute for the traditional opiate. Called "intellectual's heroin" by one drug expert, the synthetic newcomer offers the same orgasmic high as heroin, but it can be from 100 to 1,000 times as potent and is usually snorted or smoked instead of injected, according to University of California, Davis, pharmacologist Gary Henderson. Similar to other opiates, fentanyl depresses breathing and, because of its potency, can be lethal.

"Twenty percent of the people buying heroin are actually getting fentanyl" says Henderson, who runs one of the only labs in the country investigating methods to detect the drug. Detection is a significant problem. The drug is so powerfull it's distributed in extremely small quantities. As with heroin, fentanyl is usually diluted in sugar or lactose, according to Henderson.

"But [unlike heroin] if you take street fentanyl and send it to the FDA [Food and Drug Administration] for analysis, [the agency] would send it backsaying it's 100 percent sugar or lactose."

Nonetheless, fentanyl is suspected in as many as five deaths last year, according to toxicologist Ann Ferreter of the Sacramento County Coroner's Office.

Those cases, along with fentanyl samples from across the state, end up in Henderson's lab at UCD. "I've had inquires about it from just about every sheriff's department in California," says Henderson, who estimates fentanyl has killed 69 drug users throughout the state in the last four years.

Fentanyl, which has been reproduced in some seven different forms, is a decidedly suburban opiate, according to Henderson. He points out that the largest confiscation of the drug took place in Ceres, a small town south of Modesto. Though the chemical components of fentanyl are widely accessible, Henderson believes the complex drug is being produced by "extremely good medical chemists using extremely sophisticated equipment."

Fentanyl is legally sold only as a prescription drug, according to Lieutenant Harold O'Kane of the Sacramento City Police, but Henderson says new forms of fentanyl are being produced continuously that are not yet illegal on the street.

So far, local drug counselors don't consider fentanyl a major drug problem. "Sacramento Valley is one of the last spots in California that's likely to see the impact of a new drug," says Scott Strain, a supervisor at the Aquarian Effort heroin detoxification center. Drug trafficking usually runs a path through Los Angeles, Oakland, San Francisco and even the San Joaquin Valley before coming to the capital, he says.

But Dennis Ding of the Bi-Valley Medical Clinic says more drugs are circulating in Sacramento and their potency has increased significantly over the last year. Ding estimates 3,000 people are actively using heroin in the area presently. "The stronger and more available the dope, the worse the threat of addiction," says Ding.

Henderson says that fentanyl, because of its power and the ease with which it can be used, could replace heroin on the street. "Fentanyl is changing the way people get high," he says.

[From the Sciences]

THE CASE OF THE TAINTED HEROIN—A TRAIL OF TRAGEDIES LEADS TO A NEW THEORY OF PARKINSON'S DISEASE

(By J. William Langston)

The patient, a forty-two-year-old drug addict, sat frozen and mute, looking more like a mannequin than a man. His arm, if raised and placed in an awkward position, would simply remain there. He could lift a limb of his own volition, but only with great concentration and effort and only at the speed of a slow-motion replay. He could also grip a pencil and move it awkwardly across a sheet of paper. His first three sentences, rendered painstakingly, struck me as an exquisite description of what it is like to be straitjacketed by your muscles, a prisoner of your own body: "I don't know why or what is happening to me. I only know I can't move. I know what I want to do, but it just won't come out right."

A debate soon developed over whether the disorder was psychological or physiological in origin. The patient had been diagnosed as suffering from "catatonic schizophrenia," but I was convinced that some uncommon neurological disease was to blame. His hands were not only rigid; when moved forcibly, through flexing or extending the elbow or wrist, they proceeded by fits and starts, like a ratchet wheel—a symptom that neurologists call "cogwheel rigidity." Since the patient was a known heroin abuser, we first suspected that he had unwittingly ingested a tainted narcotic. However, I had never seen anything like this linked to a street drug.

The plot thickened when we learned that the patient's thirty-two-year-old girlfriend was in an almost identical state. Apparently, both had been injecting a new "synthetic heroin." Now she sat motionless, without facial expression, without even blinking. Each morning, her mother or sister would bathe her, dress her, then seat her in a chair. Three times a day, she was fed. At day's end, she was undressed and put back to bed. There is no telling how many times this extraordinary cycle would have been repeated had we not stepped in.

Careful examination of both patients revealed nearly every symptom of severe Parkinson's disease. Their general immobility, along with the telltale cogwheel rigidity, had already led me to suspect as much, but it still seemed an unlikely diagnosis. Parkinson's disease usually strikes after age sixty and almost never before age fifty. Further, the disease begins gradually, almost imperceptibly. These patients were young and had developed symptoms virtually overnight.

On that busy Friday in July of 1982, we could hardly have guessed the implications of what we were seeing. The story that was to unfold would lead us through the back streets of the northern California drug scene, into the pernicious new world of "designer drugs," and, ultimately, to a new theory about the origin of Parkinson's disease and new hope for its treatment and prevention. The line of inquiry triggered by those two drug addicts in San Jose could, with time, shed light on other diseases of aging and perhaps on the aging process itself.

Parkinson's disease is one of the two great neurodegenerative diseases of the aged. (The other, Alzheimer's disease, entails progressive loss of memory and general mental deterioration.) It is estimated that nearly half a million Americans have Parkinson's disease, including one of every hundred people over the age of sixty. Its past victims are thought to include Mao Tse-tung, Francisco Franco, and Adolf Hitler. The disorder was first described by James Parkinson in 1817. The classic triad of symptoms comprises slow movement, rigid muscles, and a trembling most noticeable in the hands (hence the name "shaking palsy"). It has been known for more than fifty years that these symptoms result, at least in part, from the death of nerve cells in a small area at the base of the brain, the substantia nigra ("black substance"). These cells, which contain a dark pigment called neuromelanin, are clearly visible in fresh-cut sections of a normal brain, and postmortem examinations indicate that they diminish steadily after the onset of Parkinson's disease. To this date, no one knows why.

Two major theories have fallen by the wayside. As a result of the great influenza epidemic of 1918–20, many people developed symptoms of parkinsonism, triggering speculation that the disease is caused by a virus. Once this peculiar strain of influenza disappeared, some predicted that as parkinsonian patients aged and died, Parkinson's disease would die out with them. This has not proved to be the case. We now know that this was an unusual variant of the disorder—postencephalitic parkinsonism. While it did indeed wane, the more common type of Parkinson's disease, seen mainly in the aged, continues to occur at a roughly constant rate. With the virus hypothesis ruled out, some theorists went to the other extreme: perhaps, they suggested, parkinsonism is hereditary—programmed in the genes, waiting to surface. But recent studies have established that this theory cannot account for the vast majority of cases. If one of two genetically identical twins gets the disease, researchers have found, the other is no more likely than the average American to come down with it.

Ironically, one of the major breakthroughs in the treatment of Parkinson's disease has in some ways retarded basic research in the field. Some fifteen years ago, neurologists discovered the therapeutic value of L-dopa, a chemical from which dopamine can be produced. Dopamine, one of the brain's neurotransmitters (which carry signals among neurons), is essential for normal control of the muscles. It is produced by cells of the substantia nigra and supplied to an area higher up in the brain known as the striatum. In Parkinson's disease, as the nigral neurons die, dopamine production drops, and the muscles freeze up. The value of L-dopa lies in the fact that, unlike dopamine, it can pass through the fluid buffer (the "blood-brain barrier") surrounding the brain. It can thus be administered to parkinsonism victims by mouth, whereupon it passes into the brain, the remaining nigral cells convert the compound to dopamine, and muscular control improves. With the advent of L-dopa therapy, patients who had been immobile for years dramatically recovered movement and were in some cases, able to function almost normally. Some patients have compared the experience to "coming back from the dead."

In the wake of this dramatic success, many doctors believed that the answer to Parkinson's disease had been found and that the rationale for research had weakened. Unfortunately, it was only a matter of time before disabling side effects began to appear, including hallucinations and exaggerated movements known as dyskinesias. Dosages of L-dopa had to be moderated, and its benefits declined commensurately. To be sure, L-dopa is a major advance in the treatment of Parkinson's disease, but most neurologists now agree that it is not the answer.

After examining our patient's girlfriend, we were still perplexed. The two had been living together. Could some household toxin, such as carbon monoxide, be to blame for their conditions? While we were immensely suspicious of the heroin, we had no evidence to implicate it. Then a timely coincidence uncovered the first in a long trail of clues that would lead with surprising speed to a solution of the mystery.

The following weekend, Phillip Ballard, a neurologist who worked with me at the time, was invited to a dinner party by an old friend, a neurologist practicing in Santa Cruz, about thirty miles south of San Jose. Somewhere between the main course and dessert, the host began to describe the case of a twenty-four-year-old man who had suddenly become as motionless "as a pillar of salt." Was the patient a heroin abuser, The answer was yes.

Here was a third and critical case. Ballard stayed overnight and the next morning examined the patient. The symptoms were identical to those of our patients. The victim and his brother had been using a synthetic heroin when both began to freeze up. It is difficult to believe, but they had continued to inject the substance until they were completely unable to move. Had their mother not stopped by their appartment several days later, they might well have starved to death.

At that point, we felt obliged to put out a public warning about the synthetic heroin circulating in the area. What began as a simple announcement turned into a full-blown press conference. For days afterward, we were inundated with calls from local newspapers and radio and television stations. Accustomed to a quiet existence, I found the sudden attention unsettling. As it turned out, though, the exposure would lead to additional clues.

The day after the press conference, we received a call from a nurse who had watched the evening news and recognized our patients' symptoms as those of a young woman she was caring for in a visiting-nurse program. This fifth victim had been completely immobile for six weeks. She had spent three of those weeks in a psychiatric ward, diagnosed as having "functional or hysterical" paralysis; she had lost all movement, it was thought, upon hearing that her boyfriend had been stricken by paralysis. But the problem, we concluded, was not in her unconscious. Both she and her boyfriend were heroin abusers. He was quickly located and found to be trembling so severely that he could no longer feed himself. Meanwhile, a chemist had analyzed the synthetic heroin used by several of the victims. A gas chromatography-mass spectrometry machine, which yields a graphical characterization of chemicals, provided a "fingerprint" of the heroin, but we found no match among some forty thousand such prints on file in Washington, D.C. The big break was still to come.

About a week after our press conference, I received a phone call from Halle Weingarten, a toxicologist at the Santa Clara County Crime Laboratory, who had received a sample of the synthetic heroin for testing. She vaguely recalled reading about a student on the East Coast who had been making his own narcotic using a formula developed in 1947 by Albert Ziering, then with the pharmaceutical company Hoffmann-La Roche. The drug, similar in effect to Demerol, was known as 1-methyl-4-phenyl-4-propionoxy-piperidine, or MPPP. Apparently, the student had taken some shortcuts and made a "sloppy batch"; shortly after ingesting the substance, he became mute and rigid. He was partly rehabilitated with L-dopa, but two years later he died of a drug overdose. An examination of his brain revealed the loss of nerve cells in the substantia nigra. Investigators never determined precisely the chemical identity of the toxin.

Weingarten mentioned in passing an article about the case in the journal *Psychiatry Research*. After reading the article, we concluded that the substance responsible for the amateur chemist's condition was 1-methyl-4-phenyl-1, 2, 3, 6-tetrahydropyridine, or MPTP, a by-product of the synthesis of MPPP. A trace too much heat or acid can turn an entire batch of MPPP into MPTP.

After reexamining our samples of synthetic heroin, we concluded that MPTP was indeed the offending agent. Evidently a kitchen chemist in northern California had been trying to make MPPP using the Ziering formula. In search of Ziering's original paper, we went to the organic chemistry department library at Stanford University. It was eerie indeed to open a 1947 volume of *The Journal of Organic Chemistry* and find that the paper had been taken, cut out meticulously with a razor blade. We then went to the Stanford medical center in search of other papers from the 1940s, only to find that each article related to the synthesis of MPPP had been removed in the same fashion. We seemed to be retracing the footsteps of an underground chemist, perhaps the one who had already ruined six lives.

We now know that the appearance of MPTP in the northern California drug market is part of a nationwide problem, the advent of "designer drugs." The term was coined to reflect the increasing sophistication of street-drug suppliers, who can now tailor their products to individual preferences regarding the nature and duration of the "high." Increasingly, these young entrepreneurs are designing drugs that differ only slightly from well-known narcotics. By making a minor alteration in molecular structure (such as adding a single methyl group or a halogen), they can preserve the psychoactive properties of the drug while moving it beyond the reach of the law; the government, after all, is required to describe precisely the structure of each controlled chemical. So, in some states, dealers can sell new variations on old drugs without fear of prosecution. Any drug deemed dangerous can be outlawed, of course, but the process can take years. Meanwhile, drug users are unwittingly serving as guinea pigs.

The chemist who inflicted Parkinson's syndrome on a half-dozen adults, though now known to local authorities, is free and, apparently, still designing drugs. The police recently arranged a visit to his laboratory; the local fire marshal inspected the house for hazards, and they tagged along anonymously. When they inquired about his abundant stock of laboratory equipment, he coolly replied that he was testing new Sno-Kone flavors.

As for his six victims: When it became clear that their symptoms were permanent, we tried L-dopa. The response was dramatic, confirming our belief that we were dealing wth either Parkinson's disease or a remarkable facsimile. In at least three cases, the L-dopa probably prevented death—a not uncommon fate for severely parkinsonian patients, who can develop pneumonia or a fatal infection. Now, two years later, all six require medication every two to three hours. Unfortunately, most are already experiencing the side effects of L-dopa. In at least three cases, the "therapeutic window" is nearly closed: if the dosage is slightly increased, complications set in; if it is slightly decreased, Parkinson's syndrome reasserts itself. There is almost no period of normality left. While this is not unusual in the final, most severe phases of Parkinson's disease, it is almost unheard of in adults in their twenties, thirties, or forties. For the moment, the future appears bleak for these young addicts.

It is no doubt small consolation that their pain may ease the suffering of other parkinsonian patients by helping to resolve a debate about L-dopa therapy. It has long been known that the side effects of L-dopa grow worse as the disease progresses. But is that because they are the cumulative effect of years of therapy, or because their severity depends on the severity of the disease? Adherents of the former view advise withholding the drug until the disease's later stages, so that the drug will still be at peak value when most desperately needed. The latter view implies administering the drug as soon as the disease is diagnosed, since the drug will not depreciate with time. It is this alternative that our experience seems to support: in our patients, who had severe parkinsonism from the beginning, the side effects of L-dopa appeared almost instantaneously.

In the February 25, 1983, issue of *Science,* we published a preliminary report on four of our patients, suggesting that MPTP was toxic to the cells of the substantia nigra. Things had settled down by then, and I was surprised when the phone in my office began ringing again. At first, we brushed aside the many inquiries as to whether MPTP might be encountered in man-made products or in the natural environment. Our patients had injected the chemical intravenously. Since most of us do not go around injecting food coloring or lake water, what did it matter whether traces of MPTP might be found somewhere in the pantry or in the outdoors? But our thinking changed rather abruptly when we received a letter from a pharmaceutical chemist who had worked for eight years during his thirties making new analgesic compounds—a job that entailed synthesizing MPTP. At age thirty-seven, his tennis game had begun to fall apart. Serves consistently went into the net, seemingly the result of his tossing the ball too low. Increasing coordination problems led him to a neurologist, and he was diagnosed as having early Parkinson's disease, which proved permanent and progressive. We are now aware of several other chemists who developed Parkinson's disease while working with MPTP. (And we have since become aware of six patients who, inexplicably, were given MPTP in the hope of *combating* Parkinson's disease during a series of drug trials in the 1950s. Two subsequently died.) It now seems clear that the compound can induce parkinsonism through skin contact or inhalation. Could unknowing encounters with MPTP or a similar substance be a cause of Parkinson's disease? It is, after all, a very simple compound. No one has systematically searched for it in the chemical refuse of our society, but it is worth noting that Parkinson's disease was first identified after the beginning of the Industrial Revolution—and that MPTP has been used by various industries, albeit in small quantities.

This line of thought raises an interesting question. If indeed the disease is caused by a chemical that, presumably, can be encountered at any age, why do symptoms usually appear only after middle age and escalate gradually? Donald Calne, a neurologist at the University of British Columbia, in Vancouver, and I have proposed a novel hypothesis for the origin of Parkinson's disease, a hypothesis that resolves this paradox. We believe that parkinsonism may be induced environmentally, perhaps by exposure to a toxin such as MPTP in early adulthood or middle age. The delay in the onset of the disease, we think, stems from the fact that one must lose approximately 80 percent of the striatal dopamine before parkinsonism sets in. During each decade of life, we lose roughly 5 to 7 percent of the neurons in the substantia nigra through aging and suffer a corresponding decrease in brain dopamine. Normally, this rate is not enough to push us across the 80-percent threshold during a lifetime. However, if half the nigral nerve cells were destroyed around age thirty, natural deterioration might well lead one over the critical line by age sixty or seventy, after which the condition would only grow worse. It could also be that the environmental insult does not destroy nigral cells immediately, but merely accelerates the natural rate of cell death. In either event, something in the environment sows the seeds of destruction on the fertile ground of aging.

But even if this theory proves correct, much will remain to be explained. Our research, along with that of other neurologists around the country, seems to raise new questions almost as fast as it answers old ones. For example, by injecting squirrel monkeys with MPTP, we induced Parkinson's syndrome, further strengthening the link between the two (and establishing an animal model of parkinsonism, an invaluable tool for future research). But no sooner had we established that MPTP is responsible for parkinsonism than we began to suspect that is not directly responsible. Studies at various laboratories have shown that MPTP, upon entering brain cells, is transformed by oxidation into an electrically charged compound, 1-methyl-4-phenylpyridinium ion, or MPP+. Whereas MPTP can penetrate the fatty lining of cell membranes, MPP+ cannot. It may be that MPTP enters the substantia nigra, is converted to MPP+ through oxidation, and then, trapped inside the neurons, begins to eviscerate them. One of our recent findings is consistent with this hypothesis. Pargyline, which precludes conversion of MPTP to MPP+, appears to prevent the destruction of the nigral neurons, as well as symptoms of parkinsonism, in primates injected with MPTP.

But of what practical value are these findings? In humans, after all, much of the damage is already done by the time symptoms of parkinsonism surface. Still, even at that stage, there is much suffering yet to be prevented—as evidenced by the experience of neurologists with another chemical that prevents the formation of MPP+. Deprenyl, long used in England for the kind of temporary relief of parkinsonism provided by L-dopa, appears to slow the long-term progress of the disease as well. This conclusion is still tentative (it is based on the retrospective evaluation of cases, not on controlled experimentation) but is certainly consistent with our findings.

However, an odd coincidence—this one biochemical—leaves open the possibility that the qualified success of deprenyl in fighting Parkinson's disease has nothing to do with MPTP. The conversion of MPTP to the apparently toxic MPP+ is catalyzed by the enzyme monoamine oxidase, or MAO, and it is by inhibiting MAO that pargyline and deprenyl prevent the formation of MPP+. But MAO, as it turns out, may play an entirely separate role in bringing on Parkinson's disease. Namely, MAO catalyzes the oxidation of dopamine, a process that, it has long been theorized, yields toxic by-products, such as peroxides and free radicals, that destroy nerve cells (and that may play an important role in the aging process). So any success of MAO inhibitors in fighting parkinsonism in humans does not necessarily implicate MPTP in the disease. Thus, we know that MPTP can induce Parkinson's syndrome in both humans and lower primates, but we have not found the smoking gun that would link it to "naturally occurring" cases of Parkinson's disease.

Still, this much we can say: the United States would do well to follow Europe's lead and, at the least, begin to experiment with MAO inhibitors—either deprenyl, pargyline, or both—in combating Parkinson's disease. If these chemicals are found unequivocally to slow or halt Parkinson's disease, they may be able to preserve a near-normal life for patients whose parkinsonism is diagnosed early.

The long-term ramifications of the past two years of feverish research into parkinsonism depend largely on the success of our theory of its origin. If indeed some environmentally induced damage to the substantia nigra, exacerbated by the natural effects of aging, is responsible for the disease, then perhaps the suffering of untold thousands can be prevented; the toxins responsible, whether MPTP or some other chemical, can be tracked down and controlled.

Further, the power of this model may reach beyond Parkinson's disease. The idea of early-to-mid-life brain damage that manifests itself only later is attracting attention in research into Alzheimer's disease and amyotrophic lateral sclerosis (ALS, or Lou Gehrig's disease), which causes paralysis. Early damage to nerve cells—spinal neurons in the case of ALS and cerebral neurons in the case of Alzheimer's disease—may take its toll later in life; Carlton Gajdusek, of the National Institutes of Health, recently proposed just such an explanation for the deadly ALS-parkinsonism-dementia complex, which has afflicted residents of Guam for years.

In the case of Parkinson's disease, this theory is about to be subjected to a test that, whatever the outcome, can only be considered lamentable. More than two hundred people who used MPTP one or more times, under the impression that it was a synthetic heroin, have now been located. Presumably, many have lost cells in the substantia nigra. Our hypothesis suggests that these patients are "walking time bombs," as one official at the National Institutes of Health put it, and will eventually display symptoms of parkinsonism. And for each known user of MPTP, there may be dozens of others who have injected the substance. So, if our theory about the origin of Parkinson's disease is correct, confirmation will come not in medical research laboratories but in emergency rooms, dingy apartments, and back alleys across California.

THE WAR ON DRUGS IS OVER—THE GOVERNMENT HAS LOST

(By Jack Shafer)

When America's Seventy Years' War on drugs began, drugs came from only two sources: plants, like the opium poppy, and pharmaceutical companies. And for fifty years the government was content to conduct only a modest campaign, seizing a few tons of contraband here, jailing a few thousand prisoners of war there. A generation ago, however, new, ultra-restrictive drug laws were added to the tough laws we already had, and the drug market struck back. Illicit drugs started flowing from a new source, clandestine domestic laboratories. Creative chemists dipped into the chemical literature and came up with a new wave of synthetic drugs that the government has been unable to stop. The net effect, tragic and ironic, of drug prohibition has been the creation of synthetic drugs that are more potent, dangerous, and unpredictable than the drugs originally banned.

If the shift to synthetics doomed the war on drugs to failure, the police haven't acknowledged it. Instead of running the white flag up the pole, they have clamored for bigger budgets, tougher laws, stiffer sentences for offenders, expanded powers—and gotten them all. But all ain't enough. The government has pushed the drug market beyond its enforcement reach. There are just too many new drugs, and too many new druggists, to stop.

Since the passage of the Harrison Act of 1914, the interdiction of drugs from abroad has been at the center of the government's strategy. But the flipside of its relative success at deterring drug smugglers from bringing in greater quantities of drugs has been the establishment of a "homemade" industry, immune to the deployment of Navy destroyers, beefed-up customs, and paraquat spraying.

Because the synthetics can be manufactured almost without detection from commonly available industrial chemicals, the supply and variety of illicit drugs is now virtually unlimitable. Just as the invention of nylon made silk stockings obsolete, the cheap synthetics stand ready to displace the organic drugs. In California the substitution of synthetics for "old reliables" like heroin has already begun. Unless we turn away from drug prohibition, and learn to live with the drugs we already have, we will be awash in a flood of cheap and deadly synthetic drug substitutes.

So forget the French Connection. Forget the Bolivian Cocaine Generals. Forget the nickel cigar. The dollar "synthetic heroin" fix is on its way.

DRUG STORY

Attributing all manner of evil to drugs and their users is a relatively new practice. Most societies in history regarded drugs as a boon. Over thousands of years, man canvassed the plant kingdom for roots and herbs to heal sickness and alleviate pain. Many of the drugs we use today are made from plants collected by early man. North American Indians discovered that tea made from the bark of a certain willow tree stopped headaches. Quinine, which is used to treat malaria, was found in the bark of the cinchona tree by the indigenous South Americans. As Aldous Huxley once said, "Pharmacology is older than agriculture."

But man's search of the plant world was never a narrow one, limited to physically healing plants. In his book *The Natural Mind,* Andrew Weil, M.D., writes, "The use of drugs to alter consciousness is nothing new. It has been a feature of human life in all places on the earth and in all ages of history. In fact, to my knowledge, the only people lacking a traditional intoxicant are the Eskimos, who had the misfortune to be unable to grow anything and had to wait for white men to bring them alcohol." Weil argues that man has an inherent need to experience altered states of consciousness, either by mediation or exercise (yoga and "runner's high" come to mind) or by ingesting drugs. Changing one's consciousness is a normal, rather than aberrant, act.

Drug use was basically limited to the unrefined plants until the nineteenth century, when chemists began isolating the active ingredients. From opium they refined morphine and codeine; from coca leaf, cocaine. But they also devised ways to modify the active ingredients to make them more potent, creating semi-synthetic drugs, like aspirin from willow bark, and heroin from morphine. Eventually, they invented wholly synthetic drugs: amphetamines, barbiturates, and heroin-like drugs such as Demerol and methadone.

Because the semi-synthetic and synthetic drugs were much more potent than the natural substances, they presented new problems for drug users. In their sourcebook on drugs, *Chocolate to Morphine,* Andrew Weil and Winifred Rosen point out that because crude plants must usually be eaten, measuring a safe dose is easy and overdosing is physically difficult, whereas purified chemicals can be introduced directly into the bloodstream by snorting or injection, which can lead to overdose or other medical problems. Also, a crude plant may contain twenty or more active components, some of which temper the effects of its principal active ingredient, an advantage not shared by refined white powders.

An early example of the problems caused by the abrupt shift from dilute to concentrated drugs can be found in mid-eighteen-century Britain, where people started tippling cheap gin instead of beer. A pandemonium of mass drunkenness went on for almost a generation until such socially moderating forces as the Methodist movement and the pub took hold. The Methodists preached temperance, and the pub owners promoted new behavioral standards for gin drinkers, looking down on drunks but up on good conversationalists.

Yet, prior to the American declaration of war on drugs in 1914, there was no popular recognition of a nationwide "drug problem." Opiates were freely available to users (except to Chinese who, as aliens, were discriminated against). You could order them by mail, get them from your doctor, or buy them over the counter. Sold under such brand names as Mrs. Winslow's Soothing Syrup and McMunn's Elixir of Opium, these widely advertised concoctions containing opium or morphine were advertised as "painkillers" and "women's friends" in magazines and on billboards. Few laws stood in the way of a user and his drugs, and throughout the nineteenth century there was no popular movement for prohibition. The opium poppy, *Papaver somniferum,* was legally cultivated and refined in America. During the Civil War opium was used freely to treat dysentery, and for intractable pain there was injectable morphine in the newly invented hypodermic needle. Subsequent addiction to these drugs was sympathetically known as the "soldier's disease."

Still, open opiate use wasn't the "done thing." As Edward M. Brecher states in the Consumers Union study, *Licit and Illicit Drugs,* opiate use was frowned upon, that is, when it could be detected. But the social stigma ascribed to it was akin to that of the vices of "dancing, smoking, theater-going, gambling, or sexual promiscuity." Only with the Harrison Act of 1914—when users were forced into a deviant, criminal subculture—did drug use begin to earn the almost universal notoriety it has today.

ANGEL DUST MEMORIES

The Harrison Act and the drug laws that followed haven't stopped people from taking drugs. The drug market simply treats the new laws as a "market distortion," as the economists would say, and the penalties and risks associated with drug dealing and use are quickly integrated into the price of drugs. Although the technology for brewing drugs in "bathtub gin" operations has been within most people's reach for decades, the ample supply of black-market pharmaceutical drugs and plants made such efforts unnecessary. But when LSD demand began to exceed the pharmaceutical supply in the mid-sixties, the first clandestine LSD chemists, like Owsley Stanley, set up their labs. His LSD was of such good quality that his name became a respected brand name on the street. By alerting others to the ease with which these lucrative drugs could be synthesized, Owsley's success kicked off the homemade drug movement, to which the government responded in its usual way: In 1966 the penalty for making drugs like LSD and amphetamine was still only a misdemeanor; two short years later it was a felony.

Though there is scant medical evidence that the illicit drugs posed greater health hazards than the licit drugs of our culture, the government's counteroffensive against drugs culminated in a set of laws even more restrictive than the Harrison Act—the Comprehensive Drug Abuse Prevention and Control Act of 1970. The law banned LSD and some other psychedelics altogether. It also erected production quotas for pharmaceutical drugs, such as amphetamines and barbiturates, that were leaking onto the black market. The new quotas quickly slashed the supply of amphetamines and barbiturates—by 1973 legal amphetamine production had been cut by 90 percent—and this created a black-market amphetamine shortage. Just as the LSD demand had been filled by LSD chemists, clandestine amphetamine chemists rose to plug this shortage.

Other drug entrepreneurs looked for exploitable drugs that had escaped the quota restrictions. One such uncontrolled drug, methaqualone, better known by its tradename Quaalude, filled the barbiturate niche. When methaqualone was brought under the production quotas and the domestic supply began to dry up, drug entrepreneurs began smuggling it in from abroad. Now they make methaqualone in their labs, along with LSD and amphetamines.

The new law also repopularized the synthetic drug PCP, or "Angel Dust." When it first appeared on the illicit market in 1967, PCP was panned by most users as an unpredictable, awful drug. Except for a small, hardcore group of users, few knowingly used PCP between 1967 and the early seventies. PCP made its return because of the confusion and shortages wrought by the new drug laws. People who wanted to get high were willing to experiment with substitutes. PCP's chameleon-like quality of acting like barbiturates at low doses and the psychedelics at higher levels filled the bill. And its low cost and the ease with which it could be made in clandestine labs weren't held against it by dealers, either. They were careful not to market PCP as PCP at first, because of its bad reputation. Instead, they fraudulently sold it sprinkled on marijuana as "super grass," or in tablets as LSD or barbiturates or any other drug a gullible buyer might want. As more chemists sprang up to cash in on the drug, PCP saturated the turbulent market. As users began to understand how to use it, many began to favor it.

By the end of the seventies the government had done everything in its power to shut PCP down. Hundreds of labs were busted, and the book was thrown at offenders. The chemicals needed to make PCP were brought under legal control. The government even conducted a propaganda campaign against the drug. Even so, PCP remains one of the simplest drugs to score on the street. The PCP episode proved that no matter what Draconian laws the government might unleash, the synthetics would always come out on top.

THE "CHINA WHITE" SYNDROME

In 1980 a new drug entered the heroin market in California. Sold as "China White," the street name for the finest Southeast Asian heroin, most heroin users could not distinguish it from the real thing [see "The 'China White' Syndrome," *Inquiry,* October 19, 1981]. It staved off addicts' withdrawal symptoms, gave users the heroin "high" they desired, and could be purchased from regular dealers. It even looked like heroin. But there were two major differences between the new China White and the old. The new China White was a clandestine lab-made synthetic, alpha methyl fentanyl. And the new China White did something its heroin counterpart rarely did: kill.

Fentanyl is the generic name of a narcotic painkiller and anesthetic marketed under the tradename Sublimaze and used in up to 70 percent of all major surgery in the United States. It is good medicine. The China White variant, alpha methyl fentanyl, is an analog, or chemical cousin of the pharmaceutical product. The compounds in the fentanyl family do not chemically resemble any of the poppy-based drugs (heroin, morphine, codeine), but they work in the brain exactly like those drugs to kill pain, induce euphoria, and, when taken repeatedly, cause physical dependence. Unlike the poppy-based drugs, the fentanyl compounds are completely synthetic and can easily be made by anyone skilled enough to make PCP or amphetamine. This makes them an ideal substitute for drug dealers wanting to crash the heroin market.

The remarkable thing about the fentanyl compounds is their potency—alpha methyl fentanyl is about eighty times more potent than morphine. Samples of China White seized by the police were about 99 percent lactose (an inert sugar) and 1 percent active ingredient—alpha methyl fentanyl.

"People die on alpha methyl fentanyl because its potency makes it difficult for a street chemist to cut," says Dr. Gary Henderson, a pharmacologist at the University of California at Davis who has been studying the fentanyl compounds for over a decade. "These drugs are effective at the microgram level," says Henderson. "About fifty micrograms will provide analgesia. About 200 micrograms might be used in surgery. At any dose above that you'd need a respirator's help. The slightest miscalculation in the lactose to alpha methyl fentanyl ratio can be deadly." (By way of explanation, a microgram is an extremely small unit of measurement. A postage stamp weighs some 60,000 micrograms.) Henderson estimates that around 300 micrograms could kill a novice addict who had not built up a tolerance to opiates. "Just a few extra crystals of alpha methyl fentanyl in the injection would be enough to cause an overdose," he says. Since this ultra-potent synthetic appeared on the West Coast in 1980, such miscalculations have killed over thirty people, and continue to kill users at the rate of about one a month.

THE DAY OF THE LIVING DEAD

Another synthetic masquerading as heroin was discovered in San Jose, California, in the summer of 1982, when George C. checked into the Santa Clara-Valley Medical Center. He lay in his hospital bed, drooling, unable to speak. If assisted, he could stand and walk slowly, but only like a zombie out of a George Romero movie. A week later his girlfriend, Juanita, came in. She too was having trouble moving. She was stone-faced and her eyes seldom blinked. These symptoms are commonly associated with Parkinson's disease, but doctors Philip Ballard and J. William Langston at first discounted that possibility. Parkinsonism is a disease that afflicts only the elderly; George was in his early forties, and Juanita her early thirties. But George and Juanita disclosed that they were intravenous heroin users, and that they had shot up some "synthetic heroin" over the Fourth of July weekend. On the morning after they had woken up feeling stiff. Swallowing became difficult for George, and a few days later he made his way to the hospital.

Ian Irwin, a drug assay chemist at the hospital, analyzed a sample of the drug and concluded that it wasn't heroin, a drug that can be synthesized from scratch but never is because of high costs. Irwin found two active ingredients in the sample: MPPP, an analog of Demerol, the popular synthetic narcotic painkiller, and MPTP, and industrial chemical with only minor opiate effects.

Since MPPP is not produced commercially, it could only have come from a clandestine lab. Homemade synthetics had struck again. The researchers discovered that whoever had been making the MPPP had formed the unwanted byproduct, MPTP, by using excessive amounts of heat and acid to rush its synthesis, and that the byproduct was responsible for the Parkinsomism In experiments, monkeys injected with MPTP have quickly developed Parkinsonism.

These were not the first cases of MPTP-induced Parkinsonism. In 1977 a Washington, D.C., graduate student in chemistry apparently made the same error when cooking his own MPPP. Recently, Dr. James Wright of the University of British Columbia reported an identical case in the *New England Journal of Medicine* in which a young Vancouveran who had made, sold, and used the MPTP-tainted "synthetic heroin" for over a year, was striken with Parkinsonism.

Nor were Groege and Juanita the only victims of the MPPP/MPTP concoction in San Jose. Dr. Langston had two medical students survey the heroin community in the area; they found that at least sixty and perhaps 120 people took the "synthetic heroin" at one time or another. Besides George and Juanita, five other local heroin users have come down with full-blown Parkinsonism, and dozens of others suffer subclinical effects. Without treatment four of Langston's patients would freeze up and die. With it, they are living on borrowed time.

Parkinsonism is caused by the deterioration of the cells in a small section of the brain called the substantia nigra, which is believed to naturally deteriorate in the aging process. But in order to exhibit symptoms of Parkinsonism, one must lose 80 percent of those cells. "Suppose people using this drug lost 50 percent of their substantia nigra cells in two or three doses—which is not at all improbable," says Dr. Langston. "If they start out with a 50-percent loss, then they could cross that 80 percent mark in five to ten years, so we might be seeing a wave of Parkinson's disease in young people in the coming years." Langston is not hopeful. "The people who used this stuff are walking time bombs."

THE ANALOGS STRIKE BACK

One of the intents of the Comprehensive Drug Abuse Prevention and Control Act of 1970 was to streamline the process of making new drugs illegal. In the heady days of the 1960s a veritable alphabet soup of synthetic hallucinogens popped out of the chemists labs and onto the street. To cope with the inventive power of the clandestine chemists, the new law made the listing of illegal drugs in the Schedules of Controlled Substances a regulatory, rather than legislative, affair. Instead of dragging a bill through Congress to ban a specific new chemical, the Department of Justice's Drug Enforcement Administration (DEA) and the Health and Human Service's Food and Drug Administration (FDA) were given the power to review and schedule new substances. This reduced by months the time needed to schedule drugs.

But the law still required the government to define drugs by their precise chemical names; so the illicit chemists came up with the analog ploy. By attaching a few new atoms to the basic PCP, amphetamine, LSD, or fentanyl skeletons, they found they could form new analogs not proscribed by law. As fast as the government added drugs to the list, the chemists came up with subtle and legal variants on the basic theme. This drove police crazy—until the analogs were listed, they couldn't make their busts stick. It frustrated the medical profession, too. Just as soon as they began to understand the effects of one drug, the law would flush another one into the open.

PCP, as usual, was on the cutting edge. With the tenacity of an insecticide-proof cockroach, Angel Dust would not go away. In reaction to the PCP crackdown, chemists spawned the legal chemical cousins of PCP—PCC, PCE, and PHP—and they crawled out of the woodwork and into the drug-abuse industry's hair. The other lab-made drugs—amphetamine, methaqualone, and hallucinogens—went the analog route, too. The DEA found itself in an arms spiral it ws bound to lose. The drug chemists had more anlogs than the DEA had regulatory ink.

The analog lesson was not lost on the purveyors of the "synthetic heroins," either. When the police finally raided the lab making the MPPP/MPTP that was causing Parkinsonism, its owner gaily told police he was experimenting with "snow-cone flavorings." Police quickly found out that even though he had enough raw materials on hand to make thousands of doses of the drug, they had no case against him, because neither MPPP nor MPTP was a scheduled substance.

China White's makers were in the clear, too. Once the government scheduled alpha methyl fentanyl in 1981, the drug makers unleashed a new analog, parafluoro fentanyl, which extended to both users and retailers the immunity to prosecution a nonscheduled substance enjoys. As long as dealers didn't represent their ware as heroin, they were breaking no drug law. (To sell *anything* as heroin, even powdered milk, violates some states' laws.)

Dr. Henderson determined that in addition to alpha methyl fentanyl and parafluoro fentanyl (as well as fentanyl itself) illicit chemists have synthesized other fentanyl analogs that he has not had the time or money to identify exactly. How many active analogs of fentanyl are possible? "That would be a good question for a graduate student to write a paper on," says Henderson. "Perhaps hundreds. Maybe thousands."

RISKY BUSINESS?

The Nazi war machine ran on diesel fuel and morphine. When the High Command's access to foreign oil fields was threatened, German scientists invented the first synthetic fuels, and when the poppy fields looked like they might fall too, the scientists invented synthetic opiates like methadone to fill any potential morphine shortage.

If the Nazis were smart enough to switch to synthetics in the face of supply problems, why hasn't organized crime? The formulas have been public knowledge for decades, but except for an illicit methadone lab busted in Mississippi in 1969, and sporadic Demerol analog production in the seventies, the evidence suggests that not many people have taken advantage of the "synthetic heroins."

That the synthetics could take over the market is clear, for the following reasons: (1) There is less criminal risk in distributing them because there are no troublesome international borders to cross. (2) Because fewer people need to be cut in on the action, the profit margin would seem to be higher. (3) The raw materials and lab equipment costs are so low that a chemist can make the equivalent of a $25 dose for less than 15 cents. (4) Until the government gets around to putting the drug on the Schedules of Controlled Substances, the manufacture, sale, and use of the drug is not illegal. (5) When the government lowers the boom on the drug, the chemist can skip on to the next active analog. (In practice, most manufacturers haven't bothered to switch to analogs because it's easier to stick with a tried and true recipe.)

Some medical authorities argue that heroin users are a fussy lot, that heroin has a special mystique to it, and that addicts would not settle for imposter drugs. That is like saying there is no room for bargain scotch because everyone wants Johnny Walker Black. Everyone might *want* Johnny Walker Black, but some who can't afford it will settle for substitutes.

The facts bear this out. The heroin market hasn't been able to taste the difference between heroin and its bargain dopplegangers. Throughout the San Francisco Bay Area, the fentanyl compounds have been successfully passed off as heroin. Many people using the fentanyl drugs don't even know they are taking a synthetic. Scores of Bay Area users enrolling in methadone clinics to shake their "heroin habits" have been surprised to be told that urinalysis shows that they are "heroin free." (Once they prove fentanyl dependency they are allowed to begin methadone treatment.) In addition to the China White disguise, fentanyl dealers are charring the lactose in their preparation to disclolor it so they can sell it as "Mexican Brown" heroin.

Druggies are in fact quite willing to shop around for "budget heroins." During heroin shortages, addicts often switch dependencies to get them through, soothing their withdrawal with alcohol and barbiturates. Many addicts have already broken the French, Mexican, and Burmese Connections by substituting strange combinations of pharmaceutical drugs for heroin. One popular substitute, "T's & blues," made up of Galwin and Pryibenzamine (a painkiller and an antihistamine) is sold on the street for about $5 a dose and gives a heroin-like high. Some users even prefer it to heroin. As the government cracked down on T's & blues, other heroin-like pharmaceutical combinations have entered the pageant. Crushed tablets of Tylenol #4 and Doriden, known as "Loads," containing acetaminophen, aspirin, codeine, and glutethimide have taken up where T's & blues left off. Another pseudoheroin, "Madame X," blends Tussionex and Doriden. This rapid substitution of one drug for another proves that the drug market is nothing if not flexible.

The brain responds to drugs because the brain itself is a drug factory, manufacturing pseudo-opiates, tranquilizers, amphetamines, and hallucinogens of its own. Medicinal chemists will eventually duplicate these endogenous substances to create what Dr. Gary Henderson calls "designer drugs," guaranteed to put you in any mood you desire for as long as you want. We are about to witness an explosion of new synthetic drugs from the pharmaceutical companies that will not only be able to mirror the effects of every illicit drug on the market—from marijuana to cocaine—but also be able to create psychoactive effects of which no one has even dreamed.

There is no doubt organized crime knows you can make synthetic replacements for heroin. They have probably avoided making and marketing a "synthetic heroin" for the same reason a gold-mine owner who has stumbled onto the alchemist's secret of turning lead into gold would guard his discovery. Consider: Both organized crime and the mine owner have a considerable capital investment in their production of heroin and gold. To switch to significantly cheaper synthetic substitutes would tip off every nickel-and-dime aspiring competitor that they no longer have a stranglehold on the market and that they are vulnerable to competition.

The rise of China White and MPPP proves that someone has kicked the sleeping dog awake. Within drug circles it is now common knowledge that a single chemist can make the equivalent of the nation's entire annual supply of heroin, without having to go to Burma or Mexico and elude customs. Dealers now know that the synthetic replacements can be made for 15 cents a dose, in forms so concentrated that the nation's annual supply can be stored in a closet, and that the supply can be distributed around the country in ordinary envelopes.

As more renegade chemists find out about the synthetic substitutes, they will gear up production and increase the supply of "heroin," and the price will drop. (In San Jose this has already happened. One of the first signals that users had that something was amiss was that dealers were willing to sell $100 worth of "heroin" for $40.) We can assume that organized crime will fight back the best way they can, knocking off the purveyors of synthetics, but, just like the cops, they will be fighting a losing battle. "Synthetic heroins" like the fentanyl compounds and MPPP are eroding their monopoly position in the heroin market, and there is little the big shots can do about it.

THE LAST DRUG SHOW

What can the DEA do to stem the synthetics that it hasn't already tried? Control the chemicals needed to make the drugs? Efforts to control the amphetamine, PCP, and methaqualone building-blocks have only impelled chemists to assemble those ingredients from more elementary chemicals—most of which can be found in any well-stocked high school chemistry lab. Bust more labs? The DEA and other police bust hundreds of labs each year, but that hasn't put so much as a dent in the PCP, amphetamine, or methaqualone supply. License lab equipment? Drugs can be made with pressure cookers, hot plates, and garden hose. Jail everyone who knows how to use a library?

If passing tougher drug laws could solve the "problem," then we would have no PCP, LSD, heroin, cocaine, or marijuana on the street. Not even Rockefeller's Draconian drug laws have shut down the open-air heroin marts in New York City, and it's hard to imagine a tougher law than Rocky's, which gives dealers of a few ounces of cocaine an automatic minimum fifteen-year sentence. International drug policy analyst, Arnold S. Trebach, author of *The Heroin Solution*, believes that harsh criminal sanctions have never worked and they will be even less effective against the new drugs. "The clandestine synthetics may well soon swamp drug markets and deliver the coup de grâce to a dying international drug system," Trebach observes.

The DEA's plans to control the synthetics may only exacerbate the problem. The DEA wants to schedule MPPP to make it illegal, but the problems posed by MPPP's improper synthesis won't be solved by scheduling it. There is, in fact, evidence that controlling drugs *encourages* their production. In the Vancouver MPPP case, the maker of the drug used the Canadian version of the Schedules of Controlled Substances as a sort of shopping catalog. Finding Demerol in the same category as morphine, he worked backward through the chemical literature to find a legal analog—MPPP. The scheduling of MPPP will alert more chemists to its existence and prompt the production of more MPTP-tainted batches. Besides, MPPP isn't the only Demerol analog. Like PCP, fentanyl, amphetamines, and LSD, it is the member of a big family.

Undaunted by scientific fact, the government is asking for the power to schedule everything in sight. In Senate bill 1762, the Comprehensive Crime Control Act, the DEA has requested emergency scheduling provisions so that it can immediately put new chemicals on its hit parade, without first consulting with the FDA. Clearly, the DEA is desperate if its idea of drug control is finding quicker ways to shut the barn door after the horse has gone.

The plain truth is that in a society as technologically advanced as ours, the government can't keep people from experimenting with drugs. Advances in chemistry made the rise of the synthetics inevitable; the government crackdown has only speeded up the process and fouled the market with drugs of uncertain purity and potency.

Instead of prohibition, which cannot work, perhaps we should try moderation. The same market forces that today provide us with pure milk and safe beer could be applied to the drug market. For those who want them, drugs would be safer to take. Drug users could come out of the criminal underground they have been consigned to for the last seventy years and live like human beings. The same socially moderating forces that helped the British control gin drinking and taught a whole American generation how to handle marijuana, could finally come into play. The only alternative is a system that creates freaky, poisonous drugs that kill and maim.

Some defend our drug laws in terms of cost/benefit analysis. The cost of drug control, including the DEA's $200 million budget and the restriction of civil liberties, is put on one side of the balance. On the other go the benefits, such as reduced drug consumption. Without a doubt, drug laws reduce drug consumption, but by how much?

In the 1880s, when there were almost no drug laws, it is believed that only 4 percent of the population used the opiates for non-medicinal purposes. Today, as psychiatrist Thomas Szasz estimates, some 35 million Americans are regularly prescribed psychoactive drugs, but because their consumption is sanctioned by the government they are called drug *users*. The tens of millions of Americans who administer drugs to themselves, on the other hand, are branded drug *abusers* and criminals because the government has not put its seal of approval on their drugs. The drug laws, in sum, have done very little to reduce total drug consumption.

The cost/benefit analysis applied to drug control fails to add up the hidden costs. As Grinspoon and Bakalar write in *The Speed Culture*, "Repressive measures may actually do more harm to the individual and society than the original 'evil,' by causing drug abusers to resort to more dangerous substances." Our drug laws have made it almost impossible to eat opium in this country, but easy to buy contaminated heroin. Coca leaves are beyond the reach of everyone, but clandestine amphetamines and adulterated cocaine can be scored anywhere. Medical researchers are denied LSD, but street PCP is readily available.

Whatever the merits of the drug laws, we must recognize that they have promoted the use and proliferation of drugs that are indisputably more dangerous. The argument that we have enough problems already with today's legal drugs without legalizing more just doesn't wash. The new drugs are here, more are on the way, and there is nothing the government can do to stop them. Only by repealing the new prohibition can we bring order to this chaos of dangerous substances, and allow the market to produce safer drugs.

But we have to act soon. Lives are on the line.

POISONING THE WELL

Besides the obvious health hazards posed by the "synthetic heroins," other clandestinely made drugs contain evil contaminants and byproducts. Some of these misformulations come indirectly from drug cookbooks like *The Whole Drug Manufacturers Catalog* and *Basic Drug Manufacture*, which are sold through the mail and in "head shops." Others come directly from the carelessness of illicit chemists in the field.

The Whole Drug Manufacturers Catalog's recipe for synthesizing methamphetamine incorrectly lists the order in which the raw ingredients should be combined; so no methamphetamine is made at all. The chemical it does produce was linked with one Texas fatality in 1981. Mercury, an extremely toxic metal, is another common contaminant in methamphetamine. A 1983 DEA study found mercury residues in 60 percent of the samples taken from twenty-five different illegal methamphetamine labs. Chronic mercury poisoning is cumulative, and, as with the MPTP poisonings, users could be doing a great deal of damage to themselves over time.

In *Basic Drug Manufacture* an alternative method of MDA synthesis deletes the final step—reduction. An inexperienced "drug chef" might assume he is serving MDA when what he is actually dishing out is nitrostyrene, another toxic substance.

In bad chemistry the "precursor" chemicals, the raw ingredients, often foul the final product. Toluidine, a methaqualone precursor, regularly turns up in methaqualone tablets. It interferes with oxygen transfer in the blood. Clandestinely made PCP and amphetamine are also often contaminated with their precursors.

Some underground chemists make counterfeit methaqualone pills in their own pill presses, stamping their tablets with the established methaqualone trade names "Lemmon 714" and "rorer 714." According to Rober Fogerson and Terry Messinger, who run the street drug identification lab at PharmChem in Menlo Park, California, some of the counterfeits are so well made you can't tell they are counterfeits until you assay them. Often there is no methaqualone in these couterfeits, and instead oen finds a mulligan stew of antihistamines, acetaminophen (Tylenol), barbiturate, cold and allergy medicines, Valium and other miscellaneous tranquilizers, and whatever else the illicit operator might have had on hand when he revved up the pill press.

Tablets marked "Lemmon 714" containing a chemical (p,p'-diaminodiphenylmetane), which doctors suspect can cause toxic hepatitis in humans, have come to the attention of the DEA's Southeast Regional Laboratory.

Cocaine and heroin are regularly adulterated with a variety of cutting agents and other drugs, which complicates intelligent self-dosing. Consequently, many of the health problems people associate with drugs actually come not from the drugs themselves, but from the polluted preparations of the black market. In a black market, users have not legal recourse if they are sold in improperly diluted fentanyl, a poisonous MPPP, or a fraudulent "Lemmon 714." Such sloppy chemistry is unheard of in the products of Upjohn, Eli Lilly, and Squibb. If drug prohibition were lifted, accountable companies could enter the market and compete to create safer drugs.

THE EFFECTS OF DRUGS

All psychoactive drugs have serious effects on metabolism and consciousness; otherwise they wouldn't be classified as drugs. Habitual use of any addictive drug, from tobacco to heroin, reduces mobility and independence. But very few of the physiological effects of drugs are irreversible or unhealthful.

More often than not, it is drug laws and not drugs, that are at the root of drug-related deaths. The laws make safe standards of purity and poitency impossible, and by driving the price of drugs up they encourage people to use hypodermic syringes, which are very dangerous, to maximize the drugs' effects. The drug debate ignores the medical effects of drugs, substituting anecdotal horror stories for scientific evidence. Here's what the experts say about the most ubiquitous drugs.

Heroin.—Even one of heroin's staunchest critics, James Q. Wilson, concedes in *Thinking About Crime* that heroin use, in and of itself, does not cause any physical debilitation. An exhaustive study of the medical literature done for Edward M. Brecher's *Licit and Illicit Drugs* failed to locate a single scientific study linking the use of heroin or any other opiate to illness.

Heroin withdrawal is nothing like that depicted in Hollywood films. According to Andrew Weil, most heroin addicts suffer no greater ill effects when deprived of their drug than you would associate with a bad case of the flu.

Heroin addicts seldom die from taking too much heroin, although that is possible. Most deaths are a result of "potentiation." In potentiation deaths, no single drug can be fingered as the cause of death; rather it is the synergistic effect of many drugs taken together that kills. A recent Centers for Disease Control study reiterates this finding by linking heroin-related deaths with the unpredictable interplay between heroin and other drugs, particularly alcohol and quinine (a drug that is used to boost the effects of heroin). Other studies have shown that both barbiturates and cocaine potentiate heroin's lethal effect. For this reason the first rule of drug taking should be "Thou shalt mix no drugs." (It should be noted that the poorly diluted fentanyl compounds *do* kill in overdose regularly, but it is possible to prepare them safely, as the pharmaceutical companies have shown.)

Cocaine.—A recent Yale University School of Medicine study found that cocaine, unlike heroin, does not lead to physical dependence, and that users cannot develop a tolerance to the drug; therefore, cocaine fails to satisfy the medical definition of an addictive drug. "Cocaine users can take the same amount of the drug day after day and get the same effect," concludes the Yale team. Cocaine overdoses are almost unheard of because the body metabolizes it so quickly. The major cocaine health problems come from radical means of administration, such as free-base smoking and intravenous injection. (See the discussion of syringes below.)

Cocaine itself does not cause any physical illness.

Amphetamines.—Habitual users lose weight and become irritable and excitable. Some call this amphetamine "psychosis." Emotional depression occurs during withdrawal. Amphetamine overdoses are exceedingly rare. The principal health problems recorded by Lester Grinspoon, M.D., and Peter Hedblom in *The Speed Culture,* are hyperpyrexia (or high fever), constriction of small blood vessels, blood disorders, and sleep problems. They also add that prolonged high-dose use may lead to mental deterioration.

Psychedelics.—"Psychedelic drugs are rarely dangerous, although some of them (especially mescaline and MDA) have a higher ratio of effective to toxic dose than others . . . and there is some chance that psychedelic drugs will activate epileptic symptoms," write Lester Grinspoon and James B. Bakalar in *Psychedelic Drugs Reconsidered.* LSD causes no more chromosome breakup than aspirin or coffee. Tolerance to LSD builds quickly, and withdrawal symptoms are nonexistent.

PCP.—Pure, pharmaceutical-quality PCP has not been available for over a decade. Street PCP is adulterated, contaminated, and inconsistent in potency. Death by overdose is rare. Most PCP deaths are a result of what the medical profession calls "behavioral toxicity," in which disoriented PCP users die in drownings, falls from high places, or in auto accidents. In *Psychedelic Drugs Reconsidered,* the authors point out that chronic users become "crystallized," that is, they suffer from lethargy and dulled thinking and reflexes. Withdrawal symptoms are sometimes noticed. There is no evidence PCP causes brain damage.

High-dose users can become psychotically fearful of their surroundings, and as adrenalin pours into their systems they are capable of the same "superhuman strength" acts as a mother who finds her child trapped under a car. The anesthetic qualities of PCP enhance this strength. Impervious to pain, a heavily dosed user pushes his body beyond the usual limits. He pays for this performance with snapped tendons and broken bones.

Barbiturates.—In *The Pharmacological Basics of Therapeutics,* Dr. Jerome H. Jaffe writes, "It has been found that 0.2 grams of pentobarbital [a short-acting barbiturate] per day can be ingested over many months without the development of any tolerance or physical dependence." Yet tolerance can be developed, and withdrawal from barbiturates can be life-threatening. Barbiturate overdoses are less common than potentiation deaths linked to barbiturate use.

Marijuana.—The medical safety of marijuana is almost universally recognized, although the drug does have its medical critics, most notably Dr. Gabriel Nahas, M.D. It does not kill in overdose and poses no greater health problems than coffee or tea. One caveat: Like tobacco, it contains tars that cause respiratory problems.

Hypodermic syringes.—People use hypodermic syringes to inject the refined white powders like cocaine, heroin, amphetamines, and barbiturates in order to get the biggest "bang per buck." Their use, then, is related to the price of drugs. When drug prices are low, there is little need to economize by shooting up. In Vietnam, up to 90 percent of American GIs who used cheap heroin smoked it or ate it. When a heroin crackdown drove the price up, users began to switch to intravenous injections.

To say that no one would use syringes if drugs were less expensive is wishful thinking. But where drugs are in short supply, intravenous use follows, and where needles are in short supply due to drug laws, users often share their "works" to cut costs. Unsterile needles spread hepatitis, AIDS, and other fatal diseases. They also cause death by embolism and do damage to veins and other tissue over years of multiple daily injections. The greatest health danger posed by hypodermic syringes is that they make it simple to put deadly amounts of drugs into the body all at once.

As Edward M. Brecher sums it up: "The one overwhelming objection to opium, morphine, heroin, and the other narcotics is the fact that they are addicting. The other disastrous effects of narcotics addiction on mind, body, and society are primarily the results of laws and policies."

THEY'RE CHEAP AND EASY TO MAKE

(By Gary L. Henderson)

DAVIS, CALIF.—Underground chemists are now synthesizing new, very potent, and potentially very dangerous drugs of abuse. These synthetic drugs have been reponsible for more than 100 overdose deaths in California alone and have caused irreversible brain damage in scores of others.

These have been popularized as "designer drugs," a term referring both to the way in which the compounds are constructed to produce very specific biological actions and the way they are marketed.

These chemists make simple changes in the chemical structure of well-established medications. Since 1979, one underground laboratory has made derivaties of fentanyl, a surgical anesthetic used throughout the world. Variations of this drug have been responsible for 100 deaths.

In 1982, someone attempted to make a designer variant of Demerol. The resulting material was contaminated with a very potent neurotoxin. Heroin addicts who used the drug were stricken with a bizarre form of paralysis, remarkably similar to Parkinsonism.

These illicit chemists take advantage of the principle that simple changes in a drug's chemical structure can result in profound changes in the drug's effects. In essence, chemists can "design in" the kind of biological activity they want. By adding or subtracting a few atoms from the basic molecule, the drug can be made more potent, longer acting, sometimes less toxic.

Present drug laws require that restricted drugs be described by their exact chemical structure. Fentanyl is restricted and can be used only by physicians licensed to prescribe narcotis. Although the derivatives produce all the effects of the parent drug—and heroin—subtle differences in chemcal structure make them new chemical entities and therefore entirely legal.

Designer drugs are not sold as synthetics but under exotic names such as "China White." In the drug trade, it appears marketing has become as important as manufacturing.

We face an enormous challenge. Designer drugs can be made cheaply and easily and sold for enormous profits. They are very difficult to detect and we know little about their biological effects and side effects. More importantly, they seem to be proliferating at an alarming rate. They are the drugs of abuse of the future.

[From the New York Times, Dec. 30, 1980]

U.S. DRUG SLEUTHS FINALLY SOLVE MYSTERY OF THE DEADLY CHINA WHITE

(By John Noble Wilford)

McLEAN, VA.—Early last month, poice in Riverside County, Calif., near Los Angeles, came upon a drug overdose victim who carried a tiny packet containing a pinch of unfamiliar white powder. A preliminary analysis ruled out any of the common drugs in the legal or illegal marketplace.

At about the same time, a deputy sheriff in San Diego County saw a body being dumped and followed the car leaving the scene. It led him to a clandestine drug manufacturing operation whose principal product was methamphetamine, or speed. On the dead body of the dumped overdose victim, however, the authorities found a tiny packet containing not speed but a white powder that could not be readily identified.

These two discoveries, seemingly unconnected at first, set in motion investigations that wound up in the hands of a little-known cadre of Federal sleuths known as forensic chemists. About 150 of these experts in investigative chemistry work for the Drug Enforcement Administration at seven regional laboratories and here at the agency's Special Testing and Research Laboratory in suburban Washington. They examine 33,000 drug samples a year, identifying them to support the prosecution of illegal drug traffickers and to assist in tracking down their sources.

The mysterious powders found in California proved to be one of the toughest cases in forensic chemistry in a long time. And it took a long time—more than a month, compared to the few hours usually devoted to sample analyses—for the laboratory detective work to produce results, which were confirmed last week.

A dangerous new substance, the Federal chemist concluded from their laboratory studies, has found its way into illicit drug traffic. A variation of the established but little-used analgesic fentanyl, it is a synthetic narcotic believed to be 80 times stronger than morphine, so potent that a dose can cause almost instant death by respiratory arrest. The injectable powder is known in the argot of the street as China White.

Agents of the Drug Enforcement Administration, an arm of the Justice Department, began hearing reports in California of traffic in the new stuff back in June. But they could not lay a hand on a sample and so had no clue as to its chemical identity or properties. They had no idea whether it was something old selling under a new name or something entirely new. All they knew was that China White commanded roughly the same prices as heroin and sold primarily in the Los Angeles area.

The two samples arrival at the agency's regional laboratory at San Diego within a few days of each other. One sample was only 20 milligrams, the other 50 (an ordinary United States postage stamp weighs in at 60 milligrams). Difficult as it was to work with such minute amounts, the chemists there quickly saw similarities between the two powders. Both were white with only a hint of pale yellow. About 99 percent of both substances was nothing more than lactose, a simple sugar. The other 1 percent defied the resolving powers of the microscope and even the mass spectrometer, an instrument that breaks up molecules and identifies the constituent parts by their energy signatures.

And so the two samples were forwarded by registered mail to the agency's special laboratory here in McLean. Stanley P. Sobol, the laboratory director, placed the highest priority on analysis of the mysterious powder because, he said, "it was new on the street" and assigned three of the more experienced forensic chemists to the task, Theodore Kram, Donald Cooper and Andrew Allen.

They, too, began with microscopic studies but could not see anything in the powder other than the lactose. Then they took a part of each sample and attempted to isolate the active ingredient through various chemical separation "washes." After many failures, they obtained enough of the isolated material to run it through mass spectrometer tests, which by bombarding the molecule with electrons gave them its molecular weight of 350.

This set some limits on what the molecule could and could not be. Using the gas chromatograph, they identified organic compounds. With the nuclear magnetic resonance spectroscope, they measured the hydrogen atoms in the molecule. With the infrared spectrometer, they examined the way the molecule absorbed infrared light to find a clue to some of its other chemical components.

DOWN THE WRONG PATHWAYS

They were identifying the possible atoms and elements and compounds that could be part of the mysterious molecule, Mr. Sobol recalled later, but the pieces did not always fit together. Impurities were "throwing us off and sending us down blind alleys," Mr. Sobol said.

Because one of the victims seemed to be associated with a methamphetamine operation. Mr. Allen recalled, the chemists sought for a few days to find in the active substance some byproduct of the synthesis of that drug. They looked, for example, into the possibility that thorium or mercury were the lethal ingredients. But no such elements showed up.

"We had ourselves a real mental puzzle." Mr. Allen said. "You think about those people out on the street. If they're putting something out, and it's killing people, it's got to be active. They're getting it somewhere so it's probably something that's listed somewhere in the scientific literature. Each day we would just have to keep piecing together what we knew or suspected and see if it added up to a recognizable molecule."

About 10 days ago, Mr. Cooper and Mr. Allen put it all together: the known constituents, such as benryl rings, the combination of carboxylic acid and amine, and the molecular weight. After trying several combinations, they drew a model of the molecule. A computerized search of the chemical abstracts showed that, with one variation, they had arrived at the drug fentanyl. What they had differed only in a single methyl(CH_3) attachment.

Fentanyl is a component of a morphine-like injection made by Janssen Pharmaceutica Inc. of New Brunswick, N.J. According to the Physicians Desk Reference, it "may cause muscle rigidity, particularly involving the muscles of respiration."

The only known legal batch of the methyl analog of fentanyl, the substance the chemist-sleuths had identified, turned out to be in the hands of Dr. Tom Riley, a University of Mississippi pharmacologist. According to the drug agency, Dr. Riley developed the substance a few years ago, in the course of research into alternative narcotics, and holds a patent on it, but it has not been produced commercially. Chemists of the drug agency believe that any competent chemist could make the substance after reading Dr. Riley's description in the chemical literature.

When Dr. Riley sent a sample of his materials to the laboratory, it was compared with the California substances, producing confirmation that the two were the same, Mr. Sobol said. Because of the impurities found in the California powder, Mr. Sobol said, the agency is operating on the assumption that the drug is being clandestinely manufactured, possibly in southern California.

From what he knows of the new drug and of other potent narcotics, Mr. Sobol said that a user would probably "get a rush" immediately after the drug's injection and then "go on the nod," passing out and becoming rigid to the point of paralysis.

Results of the chemical analysis were reported back to the California authorities, and in the January issue of the drug agency's monthly newsletter Microgram all law enforcement organizations will be alerted. Methods of identifying the compound will soon be published.

So far, the drug has been identified only in the Southwest. George R. Halpin, acting regional director of the Federal drug agency in Los Angeles, said that the new drug was apparently responsible for several other overdose deaths or hospital admissions in Southern California and also Phoenix, Ariz.

A coroner in Santa Ana, Calif., who reported six recent unexplained deaths, was sent samples of the methyl analog of fentanyl last week to see if he could establish a definite cause-and-effect link. Because such small doses of the drug can cause death and because so little is known of how the body metabolizes the drug, medical examiners have so far been unable to detect signs of the substance during autopsies.

As Federal drug agents and California police stepped up their search for the sources of the China White, the forensic chemists turned their detection scales to a backlog of other, more routine cases. The challenge of identifying a new drug from the street comes no more than once or twice a year.

[From the San Francisco Chronicle, Dec. 31, 1980]

A New, Deadly Drug in State

(By Stephen Magagnini)

A deadly new drug that authorities say is 80 times more powerful than morphine or herorin is spreading throughout California.

The drug—a synthetic narcotic known as fentanyl—has claimed a dozen lives, including two in Monterey County, since it surfaced in Southern California lst summer, say federal Drug Enforcement Administration officials.

"It's one of the scariest new drugs on the market in a long time," said Richard Dunagan, special agent in charge of the agency's San Jose office and a 23-year veteran of drug wars.

Fentanyl is sold in powdered form and is snorted or injected, like heroin. Its euphoric effects is similar to that of heroin and is fact being passed off on the street as "China White," the exotic Southeast Asian variety considered to be the Cadillac of heroin, Dunagan said.

Fentanyl—besides being "80 times as potent as any morphine or heroin on the market"—is faster-acting than China White, lasts twice as long, is difficult to trace in urinalysis and is powerful enough to overcome the "blocking" effects of methadone, Dunagan said.

"It's not heroin and it's not from China, but it is white," said Mark Hopkins, a drug counselor at the Sandborn Clinic in Salinas.

Because of its potency, street-variety fentanyl is less than 1 percent pure. But fentanyl is difficult to "cut," or dilute, so some users are purchasing much higher concentrations than others. "It doesn't cut very well—that's why people are dying," Hopkins said.

Fentanyl's long-lasting effect also can be fatal, Hopkins said. A fentanyl high can last up to four hours, while the common antidotes to overdoses of heroin and other narcotics wear off after a couple of hours, he said. Like a heroin overdose, too much fentanyl can paralyze the respiratory system.

The dozen deaths attributed to the drug have occurred in Orange, San Diego, Los Angeles, Riverside and Monterey counties, and Phoenix, Ariz., DEA officials said.

Bay Area narcotics investigators say they have seen no evidence of the drug so far, but Dr. Darryl Inaba of the Haight Ashbury Drug Detox Project said yesterday that some local addicts have been using fentanyl for several months. "A good half of our clients—30 to 40 people a day—are claiming to be using the new China White," he said. But he believes many of them actually are using fentanyl.

Once the drug appeared in Southern California, it took federal experts in Washington, D.C. several months to identify the substance.

Fentanyl was developed several years ago by Tom Riley, a University of Mississippi pharamcologist who published his methods in a scientific journal. Ironically he was trying to develop an alternative to methadone and other narcotics.

Any competent chemist can make fentanyl, a fact that Inaba called "ominous for drug users nationwide."

Dunagan compared Riley's creation to a "Frankenstein's monster—a user's chances of surviving are minimal."

In November, two know drug addicts in Pacific Grove a coastal community of 20,000 near Monterey, died from overdoses of fentanyl, said Pacific Grove police detective Bill Kennedy.

In the past three months, there have been at least 15 or 20 non-fatal overdoses of fentanyl in Monterey, County, law enforcement officials reported.

Last week, a staff sergeant at Fort Ord died of a drug overdose that may have been fentanyl, said Alexander Kerekes of the base criminal investigation unit.

The drug—which sells for as much as $600 a gram, six times the price of China White—"is very fast-acting." Kennedy said. "Addicts don't even remember taking the needle out of their arm."

Federal authorities believe fentanyl is being manufactured at an underground laboratory in Southern California. But there may be a clandestine manufacturer in Monterey County as well, Kennedy said.

UNIVERSITY OF
Miami
SCHOOL OF MEDICINE

July 16, 1985

Senator Lawton Chiles
250 Russell Building
Washington, D.C. 20510

Dear Senator Chiles:

Currently we are investigating the death of a Navy Petty Officer who seems clearly to have died of an accidental drug overdose. Some of our preliminary tests indicate a derivative of Fentanyl and thus we suspect that he died of a "Designer Drug".

Currently we also have eight (8) other deaths of which we have some suspicion of "Designer Drugs". These shall remain a suspicion for we have found levels of others drugs to explain the deaths.

"Designer Drugs", particularly derivatives of Fentanyl, are a nightmare for those of us charged with determining the causes of death of people who die suddenly and unexpectedly. The minute amounts capable of producing death are very hard to find. Thus we suspect more deaths are occuring than are being reported.

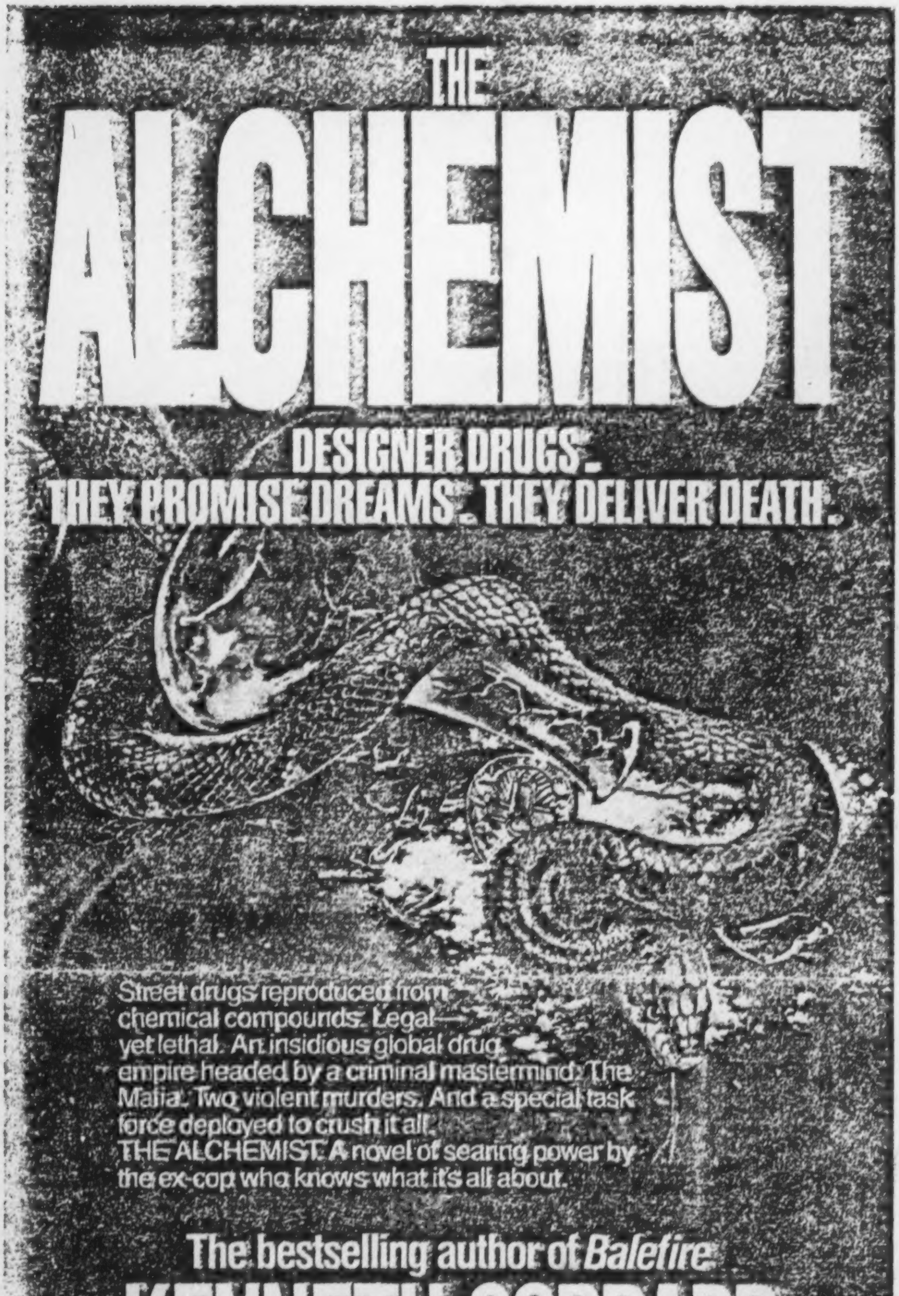
At any rate, we would appreciate whatever the Federal Government might be able to do to reduce or eliminate "Designer Drugs" from this country.

Sincerely,

RONALD K. WRIGHT, M.D.
Chief Medical Examiner

RKW:cll

Broward Medical Examiners Office
Department of Pathology
Division of Forensic Pathology
5301 S.W. 31 Avenue
Ft. Lauderdale, Florida 33312
Dade (305) 620-0017
Broward (305) 765-8590



THE ALCHEMIST

DESIGNER DRUGS.
THEY PROMISE DREAMS. THEY DELIVER DEATH.

Street drugs reproduced from chemical compounds. Legal—yet lethal. An insidious global drug empire headed by a criminal mastermind. The Mafia. Two violent murders. And a special task force deployed to crush it all.
THE ALCHEMIST. A novel of searing power by the ex-cop who knows what it's all about.

The bestselling author of *Balefire*
KENNETH GODDARD
A BANTAM HARDCOVER

NBC Nightly News

WITH

TOM BROKAW

TUESDAY, FEB. 19, 1985

NBC NEWS

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Gary Young believes the families who survive on their land may well be those who practice an old-time virtue: self-reliance. Bob Dotson, NBC News, Cedar County, Nebraska.

HIT: 7:17:35

HIT: 7:17:42 COMMERCIAL

HIT: 7:19:13

TOM BROKAW: This was a big day for artificial heart patients Murray Hayden and Bill Schroeder. Hayden got his plastic heart only three days ago and today he asked to watch television. He also sat up and exercised. His doctors call his progress spectacular.

For his part, Schroeder took a wheelchair ride to visit Hayden. That seemed to perk him up. So, today, the doctors let Schroeder take a brief wheelchair into the hospital's sunny parking lot.

There is no health benefit, however, to be gained from taking so-called designer drugs. People take them to get high in several different ways, and David Burrington reports tonight that these drugs are not only cheap, they're legal.

HIT: 7:19:53

DAVID BURRINGTON: Sophisticated California chemists are designing synthetic heroin that's so potent, some addicts prefer it to the real stuff.

MAN: It's better. It's definitely better as far as the rush and the high is concerned.

BURRINGTON: It's also cheaper. So, sales are booming. At least twenty percent of California's heroin addicts are now believed to be buying the so-called designer drugs.

MAN: I think heroin will gradually phase out as more and more illegal labs start to make the designer narcotics.

BURRINGTON: Many of the narcotics are not yet illegal. They're so new, they're not regulated by federal law.

The chemists take a known drug, like phentonol, a prescription painkiller used in most major surgery, and change a molecule. That creates a new narcotic. There are hundreds of possible variations, and some are far more powerful than heroin.

MAN: You want to tear(?) the potency, the duration of action, limit the side effects, to do just about anything you want; you can design it to be smoked, or mixed with a martini, a businessman's special.

BURRINGTON: At least seventy-seven addicts have died from overdoses of synthetic heroin over the past five years. Another seventy-five have developed signs of Parkinson's disease from an impurity found in one new drug. It's feared many more will develop the disease. But warnings have not had much effect, and some experts see synthetic heroin as the problem drug of the future.

MAN: I think it will flood the country. Why wouldn't it? They're cheap. They're easy to make. And you can make uncontrolled versions of them. I see a huge and I'm not sure stoppable problem.

BURRINGTON: Designer drugs don't have any borders to cross. So, they present federal drug officials with a major challenge, and organized crime with a major opportunity. David Burrington, NBC News, San Francisco.

HIT: 7:21:10

TOM BROKAW: John Chancellor is here with tonight's Commentary now, talking about these big libel trials, the losers and the losers.

HIT: 7:22:01

DESIGNER DRUGS

[Extract from NBC TODAY, Mar. 26, 1985]

PAYTON: I got bored with her getting up at the crack of dawn Saturday morning and coming back at sunset and falling asleep because she's had a big day chasing the foxes all over the countryside, so, I learned how to ride, four years ago, and took to it. And I got to tell you that is -- of all the things I've done in my life, the most thrilling thing I've ever done is get on a horse and go jump over a fence. Not to catch the fox. It's really between me and the horse and the countryside.

DAVIS: For Today, Rick Davis, NBC News, near Duddington, England.

PAULEY: And we'll have another look at an American abroad, tomorow -- one who made it big on Italian TV. Coming up next, on After 8, The Deadly World of Designer Drugs. But first, this is Today, on NBC.

HIT: 8:14:33

COMMERCIALS

HIT: 8:16:41

GUMBEL: On After 8 this morning we look to the latest drug threat, designer drugs, chemical relatives of drugs designed to produce the euphoric effects of narcotics. The synthetics are perfectly legal, and can prove lethal. In California, so far, designer drugs have claimed the lives of at least 87 users, and many others who got their high-tech high now suffer permanent neurological damage.

This chemist at California's Institute of Medical Research is studying the effects of synthetic heroin. For research purposes, he took Fentamil, a well-known prescription drug commonly used in surgery. He redesigned its chemical structure to make a new narcotic.

MAN: It's two-step synthesis on the order of approximately a day of work in the laboratory.

GUMBEL: Designer drugs are easy to manufacture, and so new they're still legal.

In this drug factory in Brownsville, Texas, these two men were found guilty of making angel dust. Authorities also found traces of synthetic heroin, but no charges could be filed. Designing synthetic heroin is not a crime, even though it can be very dangerous.

At Santa Clara Valley Medical Center, this former heroin addict is undergoing neurological tests. He's suffering the degenrative effects of Parkinson's disease caused by synthetic heroin. Another patient, a prison inmate, asked not to be identified but admits he took designer drugs, too. He is also suffering from early signs of Parkinson, but even that might not stop him.

MAN: You still would use it.

MAN: Yeah.

MAN: Uh-huh?

MAN: Yes. I mean, I'm a heroin addict. You know, I mean, a heroin addict don't turn down a high.

GUMBEL: Joined in the studio here in New York by Dr. J. William Langston, who is chief of Neurology at Santa Clara Valley Medical Center, in San Jose.

And good morning to you, Doctor. These designer drugs --are they being used by druggies or people who don't want to be throught of as druggies?

J. WILLIAM LANGSTON: I'd say both. It's a problem that we think is starting to permeate the entire drug market.

GUMBEL: Why are they so much more deadly than the usual fare? Or are they?

LANGSTON: Oh, I think they potentialy are. The big problem is that these illicit chemists, who are getting very sophisticated, are attempting to escape the law by redesigning well-known narcotics, or other drugs, really. But when they make new drugs, they don't have to test them on animals, like a drug corporation, a pharmaceutical corporation would. So, the first people to try them are addicts on the street. If they've got a good one, it's a winner, but sometimes they're poison. So, anybody who uses these new drugs -- they're playing a form of Russian roulette, really.

GUMBEL: Yeah. Let's get the official government word on these things.

Joining us this morning in Washington is Gene Haislip. He is in our Washington. He's Deputy Assistant Administrator for the Drug Enforcement Administration.

Mr. Haislip, what's the D.E.A. been doing about these drugs?

GENE HAISLIP: Well, this has been a problem for several years, Bryant, and I think that the doctor has described it very well. What we have done, last year, as part of the President's crime package, we asked the Congress for the power to put these drugs under control on an emergency basis when we identify problems with them.

GUMBEL: You can make them illegal -- what? -- in 30 days, right?

HAISLIP: That's correct. In fact, we published a notice yesterday on one of these drugs that has been responsible for a number of deaths in the California area. That particular drug will be under control with the expiration of 30 days.

GUMBEL: But does that get it done? Now -- and maybe the doctor can correct me if I have my facts wrong, but, by restructuring the formula, if you declare one illegal, can't they simply turn around and make another one that is legal?

HAISLIP: This is a possibility. But previously, it would take us perhaps a year or longer to react to changes of that kind. Now, at least, we have a legal capability to react in a much shorter timeframe than was previously the case. This is new legislation. We don't know if it's going to solve the problem. But I think that it's definitely going to change the situation for the better.

GUMBEL: Hmm. Dr. Langston, what more would you like to see done?

LANGSTON: Well, I think a very active intervention after it, an attempt to monitor what's going on out there, to identify these as quickly as possible. I think the control legislation is a good step.

I certainly hope the one he refers to is the one we've been dealing out -- with at Santa Clara Valley Medical Center, which is a -- causing this Parkinson disease-like syndrome. It's a permanent neurologic damage these people have suffered. That one, I think, has to stop, because it's so dangerous.

GUMBEL: Um-hmm. Dr. Haislip, why have these drugs for the most part been restrictedto California? How do you explain that?

HAISLIP: California has had a history of this type of pattern in its drug problem. If you recall, California is where the problem with LSD and many of the other so-called clandestine laboratory drugs really began. It seems to be a group of people out there, or sort of a drug subculture, that's responsible for this activity, and it's in line with that tradition.

GUMBEL: Yeah. Any way of preventing the proliferation of these things, Dr. (UNCLEAR), quickly?

LANGSTON: Boy, I wish I knew! These things seem to proliferate faster than you can identify them. And that's the name of the game, and how they're going to stop it, I -- it's going to be difficult.

GUMBEL: Gene Haislip, thank you for joining us, in Washington, and Dr. Langston, J. William Langston, here in New York. Thank you both, gentlemen, for the warning.

HAISLIP: Thank you.

GUMBEL: A story we'll continue to watch.

Eight-twenty-two -- the hour moving past, this Tuesday morning. We'll come back. Much more, ahead. But first, a break. This is Today, on NBC.

HIT: 8:21:49

COMMERCIALS

HIT: 8:24:00

U.S. Department of Justice
Drug Enforcement Administration
Office of Science and Technology

Microgram

Published by the Drug Enforcement Administration, Forensic Sciences Division, Washington, D.C. 20537

The Assistant Attorney General for Administration has determined that the publication of this periodical is necessary in the transaction of the public business required by law of the Department of Justice. Use of funds for printing this periodical has been approved by the Office of Management and Budget through March 26, 1981.

Dept - Solvent [illegible]

VOL. XIV, NO. 6 JUNE 1981

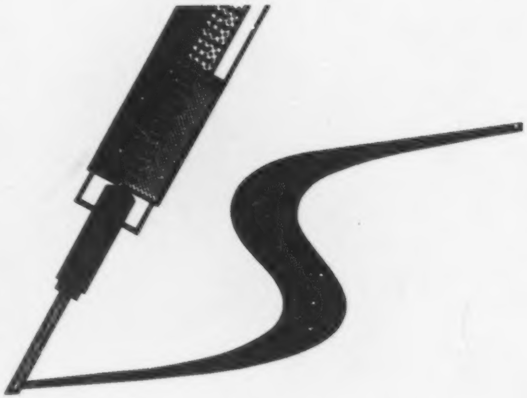
DEA South Central Regional Laboratory in Dallas, Texas has identified alpha-benzyl-N-methylphenethylamine 31% in an exhibit also containing methamphetamine 41%. The exhibit, which was submitted by the Bexar County Crime Laboratory, was implicated in an overdose fatality. Alpha-benzyl-N-methylphenethyamine is a byproduct of synthesis of methamphetamine, and is not controlled under Federal law.

Latest encounters with alpha-methyl fentanyl reported to DEA include two exhibits submitted to the DEA Southwest Regional Laboratory in San Diego, California by the Huntington Beach Police Department in that state. As in the past, the exhibits contained mostly lactose, with the active ingredient being present in trace amounts. Alpha-methyl fentanyl was also identified by the DEA Special Testing and Research Laboratory in an exhibit seized by New Jersey State officials in connection with a clandestine laboratory which had exploded. The laboratory was apparently engaged in the synthesis of phenyl-2-propanone from phenylacetic acid and sodium acetate. Alpha-methyl fentanyl was present at an extremely low level of concentration. No determination could be made as to whether the laboratory was producing this compound, or whether it had been added to the exhibit elsewhere. DEA is in the process of preparing a recommendation to the U.S. Department of Health and Human Services to control alpha-methyl fentanyl in Schedule I of the federal Controlled Substances Act.

CAUTION This publication is restricted to forensic scientists serving law enforcement agencies

Designer Drugs

The New
Bad News
About
America's
High-Tech
Highs



A D.I.N. PUBLICATION BY CHRISTINA DYE

No-Name Brand Names

It's the latest passion in fashion. And it's everywhere all at once—on jeans and jewelry, panties and perfumes, shirts, shoes, and sunglasses. And most of us know the names better than we know our own next door neighbors: Bill Blass and Calvin Klein, Yves St. Laurent and Oscar de la Renta.

But while status-conscious consumers consider the tell-tale designer label to be *de rigeur* in everything from clothes to cosmetics, there's still one place you won't find a designer ID. And that's on—or anywhere near—the chemical creations of America's high-profit, low-profile illicit drug manufacturers.

But even if no one *ever* knows the name behind the nudge in chemical high chic, drug chemists don't seem to mind, just as they never seem to tire of tinkering with tried-and-true drug recipes. And they never *ever* seem to tire of *that*—endlessly searching, like modern-day alchemists, for ways to turn base chemicals in the lab into gold on the streets.

What their searching has turned up in the last couple of years is a new generation of street drugs—a group of chemicals dubbed "designer drugs" because of their teased-up, tinkered-with chemical formulas. And while designer drugs thus far have defied convenient chemical classification, they're fast defining what's "in"—and, increasingly, what's available—in drug styles from Harlem to Honolulu.

But unlike followers of fashion, users who try on designer drug lines often pay for more than just the product's punch. Many also buy a brand-new breed of problems along with the drugs—problems linked to the sheer number of unknown factors surrounding drugs so new they don't even have names—*or* laws against them yet. And a growing number of users are discovering—the hard way—that when they buy designer drugs, they're paying a lot more than they bargained for.

Kitchen Chemistry

Or Building the Better Psychoactive Bullet

What drug fashion followers *are* paying for is the latest technological triumph in making—and marketing—illegal drugs: synthetic look-alike and act-alike spinoffs, called analogs, of high-demand drugs like heroin. Chemically designed to sidestep restrictions on their sale and use, the synthetic analog line is quickly shaping up to be a new main line on American streets. And with good reason.

Because since the earliest days of the mid-60s recreational drug explosion, profit-minded drug merchants have searched for ways to feed the voracious American appetite for increasingly-illegal drugs without the bother of shipping supplies into the country or slipping them under the nose of canine-backed customs patrols.

So they started making their own.

Probably the best-known of the early chemical whiz kids was legendary LSD chemist Augustus Owsley Stanley III, who, between 1965 and his arrest in 1967, manufactured uncounted millions of doses of connoisseur-grade LSD. During his brief reign as "Mr. LSD," the "Owsley" brand name served as *the* name in designer acid on two continents.

Many of the chemicals turned out to be legal—simply because they never existed before, or at least not long enough for someone to pass laws against them.

But while Owsley was probably the last drug-lab operator to push his products (and his luck) under a personal "label" (other chemists sagely noted that this practice led to unwanted attention from local police), he represented something more than just a one-time blip on the seismic flow-chart of illicit drug history. Far from being an end point or a mere curiosity, Owsley was really the first of a new breed of drug capitalist, the grassroots enthusiast-entrepreneur.

And while Owsley was first, he certainly didn't turn out to be last *or* most successful—not if you measure him against the hundreds of self-styled drug chemist-evangelists who came after. Because their operations—and their make-it-in-the-USA attitude—made Owsley and his modest mission look positively pale by comparison.

Because along the way, drug makers discovered they could make a lot more than just LSD in backstreet labs. In fact, many learned to squeeze an almost-endless parade of subtly-different preparations from a single chemical formula simply by switching a few molecular links in a drug family chain. And the analogs they produced suddenly emerged as ideal, low-cost replacements for exotic imported drugs.

Manufactured in make-shift labs by anyone with a small investment in glassware and a nodding

Taking It To The Street: An Analog Update

Fentanyl and MPTP are only the most recent additions to the ranks of "new and improved" products from the nation's illegal drug labs. Because the designer drug-analog phenomenon has been around nearly as long as the backstreet drug business itself and includes synthetic spinoffs of most high-demand illicit chemicals.

Other frequently-found drug analogs include:

- ***Phencyclidine (PCP)* analogs such as PCE, TCP, PHP, and PCC, all of which carry a more powerful punch than phencyclidine. PCC, particularly, is associated with unpleasant reactions and bad trips.**
- ***Short-Acting Tryptamines*, including the hallucinogen DMT and its analogs DET and DPT, were rarely seen on the street until the early 1980s when DEA lab seizures recorded a 200% increase in DMT/DET-making operations. The compounds are best known for their sudden, intense effects, which make driving—or even standing around waiting for something to happen—a dangerous undertaking.**
- ***Amphetamine-Based Hallucinogens* include the family of synthetic compounds related to MDA and MDM. The best-known chemical relatives—PMA, TMA, DOM (or STP), and DOB—are also the most dangerous. PMA and DOM are highly toxic and can trigger prolonged mind-bending hallucinations. DOB, sometimes sold as LSD on squares of paper called "Golden Eagles" or "tiles," is linked to blood vessel spasms that can reduce blood flow to the extremities.**

acquaintance with chemistry, designer drugs carry few of the risks of international smuggling. For one thing, there's none of the high overhead—and high risk—associated with moving a plane or boatload from There to Here. For another, many of the chemicals turned out to be legal—simply because they never existed before, or at least not long enough for someone to pass laws against them.

All of which adds up to a high-profit picture for anyone with an extra $500 in their pocket and a college chemistry class or two under their belts. But it also adds up to problems for people who buy and use the new home-made highs. And since the designer analogs first hit the streets, *that's* added up to quite a few problems for quite a few people, indeed.

Real Killer Dope:

The Fentanyl Family

In 1980, the first serious wave of problems linked to designer drugs got as bad as problems can get. A new "synthetic heroin" turned up on the West Coast and swept the streets from San Francisco to Phoenix before Drug Enforcement Administration investigators tracked it down some 10 months and 30 overdose deaths later.

Sold as "China White," an ultra-potent form of Southeast Asian heroin, the mystery compound was an almost perfect stand-in for heroin. *Almost* perfect. It *did* satisfy junk cravings and it did stave off withdrawal. The yellowish-white powder even *looked* like heroin, and although it didn't leave the characteristic bitter tang on the tongue, the powder *did* fool the experts for a while, until blood and urine samples from overdose victims kept coming back clean in tests for opiates.

DEA chemists went to work on the "heroin" and discovered that the drug wasn't an opiate-based narcotic at all, but alpha methyl fentanyl (AMF), a little-known and easily-synthesized relative of the surgical anesthetic fentanyl. The discovery—and the overdose deaths—were duly written up in the press under the usual (though suddenly very real) "killer dope" headlines, while alpha methyl fentanyl was quickly labeled a new "drug of abuse" and placed in the most restricted category of federal controlled substances in September 1981. Then the whole incident quickly passed from the public mind.

But fentanyl's street story was just beginning. AMF is just one of an estimated 1,400 different analog combinations in the fentanyl family that can easily be synthesized in illicit labs. In fact, it's almost impossible to miss in making the drug since any slight chemical turn off the basic fentanyl molecular skeleton will still produce a highly-potent, highly-individual, brand-new, never-seen-before synthetic narcotic.

And potency is the fentanyl family name. The parent drug, fentanyl, is some 50-100 times more potent than heroin. AMF is roughly the same strength while 2-methyl fentanyl (the next compound over on the family chain) is slightly stronger. Three-methyl fentanyl, the most powerful of known fentanyl analogs, is considered 500-2,000 times more potent than heroin, while the potency of yet another family member, para-fluo fentanyl, is still unknown.

Fentanyl's potency alone is cause for serious concern for most users, particularly given the lack of quality control (and honesty in advertising) that's long characterized the drug marketplace. Still, other factors add up to an even more frightening picture. For one, fentanyl compounds are simple to synthesize. Too simple. About $200 worth of precursor chemicals can produce a two-year supply that retails for up to $2 million. For another, the high potency of the drugs makes it difficult to dilute a dose down (using standard drug bulking agents, such as lactose or milk sugar) to a manageable—and safe—consistency. Even a few too many *micrograms* of a fentanyl compound can add up to a few days in the hospital, and given that most "China White" samples in 1981 were found to contain only 1 percent AMF along with 99 percent filler, finding a safe level of drug-to-filler can be extremely tricky. And because fentanyl's respiratory-depressant effects are longer-lasting than its narcotic effects, when overdose *does* occur, it requires fast medical attention.

Sometimes the drug's a hit and everyone's happy. But other times it's a complete miss and there's no one even around to complain.

Since fentanyl and its chemical cousins are easy to make and produce such an euphoric tangle of heroin-like effects, the compounds are ideal candidates for enterprising drug chemists who want to crash the heroin market. So far, widespread use of the drugs appears limited to the West Coast, although no one is certain that it hasn't spread further since standard drug detection tests are not sensitive enough to spot fentanyl analogs.

In fact, there doesn't seem to be *any* real way of tracking down fentanyl. Experienced heroin users say the drug's initial rush is milder than heroin's, but novice or weekend users aren't likely to notice a difference. The most obvious clue to the chemical content of a suspicious street heroin purchase is that, unlike heroin, fentanyl compounds are water soluble and will dissolve without heating.

Predicting potency of fentanyl or other available designer creations is another thing, entirely. That's because determining potency is a hit-or-miss "science" in the street chemistry business in the first place, one sometimes settled simply by dishing out samples to unknowing "test subjects" and waiting to see what happens. Sometimes, as was the case with Owsley's legendary LSD, the drug's a hit and everyone's happy. But other times it's a complete miss and there's no one even around to complain.

Worse than Killer Dope:

The MPTP Story

In mid-1982, a California-based chemist missed. By a long shot.

Working backward from a government listing of synthetic painkillers, the chemist hit on a still-legal psychoactive analog of Demerol, a prescription compound used to relieve moderate pain. Impatient with the slow "cooking" time needed to produce the analog (known in tongue-twisting chemical nomenclature as 1-methyl-4-phenyl-4-propionoxy-piperdine, or M3P), he added extra acid and turned up the heat to speed processing. The shortcuts backfired. But no one knew *that* until unwitting users shot up the sloppy "synthetic heroin" (also sold as "new heroin" and "China White") and succeeded in short-circuiting their central nervous systems.

Because what slipped out of his lab and into hypodermic needles across northern California was an unwanted chemical contaminant called MPTP (short for 1-methyl-4-phenyl-1,2,5,6-tetrahydropyridine). And what *that* spells for the more than 150 heroin users known to have tried the drug is an incurable syndrome similar to Parkinson's disease: permanent and progressive brain and nervous system damage and almost complete paralysis.

In fact, MPTP-related damage to nerve tissue was so rapid that some unlucky users were found paralyzed with needles still stuck in their arms. More typically, though, "new heroin" users suffered the equivalent of decades' worth of brain damage in two or three doses. The typical syndrome starts with a cluster of arthritis-like symptoms, including stiffness, tremors, seizures, and difficulty in speaking, appearing 2-10 days after use.

The "synthetic heroin," described as a sticky, brown grainy powder, surfaced again in late 1983 and, thus far, cases of drug-induced Parkinson's disease have been reported as far away as British Colombia. Outside of full-scale laboratory analysis, the only known way to identify the drug is by the burning sensation it leaves during injection. But for the hundreds (or thousands) of "synthetic heroin" users that experts predict will stumble across the analog by late 1985, by that time it's often too late.

New, Not Necessarily Improved

Probably the most frustrating aspect of the entire designer drug phenomenon is the large amount of uncertainty involved. No one has any real idea of how many possible, weird, new one-step-ahead-of-the-law chemical concoctions are out there or are likely to turn up in the future—*or* how many users will be burned—or worse—sampling home-made highs.

Plus, the problem doesn't seem to be going away. That's probably tied to the fact that the biggest part of the "War on Drugs" technology is directed at intercepting smugglers on the high seas rather than capturing chemists on America's backstreets, which means it's faster, cheaper, and safer for drug merchants to make their own, whenever their own can be made in the U.S.A. And drug dealers *always* go for what's fast, cheap, and safe—at least for themselves.

Probably the best advice we can offer users is the oldest advice on the streets: Be careful. Drugs have always been dangerous *enough* in the first place; today's new breed of no-brand designer chemicals threatens to take those dangers to an entirely new—and unpredictable—level.

Because as too many unsuspecting users have discovered, "new" doesn't always mean "improved" and "designer" doesn't always mean "better." All it really means is that you pay, sooner or later.

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NEUROLOGIC COMPLICATIONS OF DRUGS OF ABUSE

J. William Langston, M.D.
E. B. Langston, M.D., Ph.D.
Department of Neurology, Santa Clara Valley Medical Center
San Jose, California 95128

Stanford University School of Medicine
Stanford, California 94305

INTRODUCTION

The purpose of this chapter is to describe neurological disorders which may be encountered in patients abusing illicit drugs. While the extent of drug abuse may vary from area to area, most physicians will see at least an occasional perplexing neurological disorder which will ultimately prove to be the result of illicit drug use. Most of the commonly encountered street drugs will be discussed, with particular attention given to specific signs or syndromes which are likely to lead to detailed neurological assessmennt. Marijuana, heroin, amphetamine, cocaine, phencyclidine, and the "new synthetics" are reviewed. The latter, now popularly known as "designer drugs", are already widespread in California and almost certainly pose a serious national problem for the future. Alcohol (a licit drug of abuse) and infectious complications of intravenous drug abuse are covered elsewhere in this book.

It is important to note that virtually all of the substances reviewed here are primarily, if not exclusively, pharmacological agents as opposed to true neurotoxins (i.e., compounds which actually cause nerve cell destruction). If it were otherwise, most would have long since lost their street popularity. The major exception to be discussed in this chapter is 1-methyl-4-phenyl-1,2,3,6-tetrahydropyridine, or MPTP. This distinction between neurotoxic and pharmacologic actions is an important one since it has direct bearing on controversies regarding long term sequellae of drug abuse.

MARIJUANA

The use of the plant Cannabis sativa for psychoactive effects has been common in the Middle and Far East for thousands of years (Richter, 1984). Its recreational use in the United States initially occurred in the 1920's and increased markedly in the 1960's. The most popular street names for marijuana are grass and weed. It may be smoked or taken orally, but smoking provides effects which are more rapid and, for similar effects, the oral dose equivalent is three-fold larger (Hollister, 1971). Cannabis contains several active chemicals, the most active of which is the trans-delta 9-tetrahydrocannabinol (delta 9-THC) (Mechoulam, 1970). The psychoactive agents are found primarily in the resin of the plant; hence, cannabis with more resin has more potent effects. Hashish is a resin extract of the plant. Marijuana is a dried mixture of all parts of the plant and contains 1-2% delta 9-THC.

Psychological effects include sleepiness, euphoria, difficulty concentrating, alteration of time sense, less discriminating hearing sense, and visual sense sharpening with many distortions (Hollister, 1971). At doses greater than 250 mg/kg, hallucinations may occur (Polson et al, 1983), as well as paranoia and irresistible impulses (Richter, 1984).

Studies on chronic abuse of marijuana in the United States, using delta 9-THC for 31 to 94 day periods, have failed to support the hypothesis of long-term central nervous system (CNS) damage (Cohen, 1976), although none of these can be considered as definitive due to various methodological limitations. Earlier reports using pneumoencephalography suggested that chronic abuse leads to thinning of the cerebral cortex and dilatation of the ventricular system (Campbell, 1971) but these radiological findings have not been substantiated utilizing computerized tomography (CT) (Kuehnle et al, 1977; Co et al, 1977).

HEROIN: A CONTINUING MAJOR DRUG OF ABUSE

In 1898, the Bayer Company of Germany created a semi-synthetic derivative of morphine which they named Heroisch (translation: large, powerful) or heroin (Ashley, 1972). Heroin is the diacetyl derivative of morphine, which is 2-3 times more potent than morphine and gives a greater euphoria and stimulation (Ashley, 1972). Current street names include China white (southeast Asian origin representing supposedly highly purified substance), Persian white and Mexican brown (which is usually sold as "organic" as opposed to "synthetic" heroin).

The effects from acute intoxication with opiates, including heroin, are well-known and only certain aspects are reviewed here. Miosis is a cardinal feature, and is probably due to an excitatory effect of the autonomic portion of the oculomotor nucleus (Lee and Wang, 1975). It also produces euphoria, analgesia and sedation. Coma due to overdose and its subsequent complications are a major cause of neurological damage in heroin abusers. Heroin overdose leads to coma with depressed respirations, increased pulse rate and miosis. Seizures may also occur (Richter et al, 1973). Upon recovery from coma, a variety of neurological complications have been observed, including acute delerium, post-anoxic encephalopathy, cerebrovascular infarctions, unilateral parkinsonism, hemiballistic movements, bilateral deafness, and infarction of the pituitary gland (Richter et al, 1973). Most, if not all, of these complications are thought to be the result of hypoxia and hypotension associated with overdose, although hypersensitivity to heroin or its contaminants may contribute. Delayed post-anoxic encephalopathy has also been reported (Protass, 1971), as has an interesting case of a delayed ventral pontine syndrome (Hall and Karp, 1973).

The neurological complications of heroin abuse, other than those resulting from overdose, include both infectious and non-infectious disorders (Pearson and Richter, 1979). Infections are primarily the result of intravenous (IV) injections using contaminated materials, and include meningitis, hepatitis, local abscesses, acquired immunodeficiency syndrome (AIDS), and the neurological complications of endocarditis, including cerebral embolization and the development of mycotic aneurysms (Richter et al, 1973; Gilroy et al, 1973).

Stroke-like syndromes are well documented in heroin abusers. While many of these are found to be a manifestation of bacterial endocarditis with embolization, other cases are more difficult to explain. Vasculitis induced by heroin has been suggested as a possible etiology in several reports (Citron et al, 1970; Lignelli and Buckheit, 1971). In a series of nine heroin addicts with cerebral infarction reported by Brust and Richter (1976), endocarditis with emboli or overdose with hypoventilation appeared to be unlikely etiologies, whereas cerebral arteritis was documented in at least two patients by angiography. However, amphetamine, rather than heroin, is considered to be the more likely etiologic agent causing drug induced cerebral vasculitis in the series reported by Citron and colleagues (1970). An interesting case of delayed onset of hemiparesis after IV heroin injection could not be explained by embolic events, intracranial hemorrhage, or vasculitis, and the underlying cause of this patient's cerebral infarction remains unknown (Woods and Strewler, 1972).

Peripheral nerve disorders have been described as a complication of heroin abuse, usually secondary to drug injections into one or more nerves (Finelli and Taylor, 1977) or from tourniquet pressure. Brachial and lumbosacral plexitis may occur with intense neuritic pain, mild to moderate weakness, and sensory deficit (Greenwood, 1974; Challenor et al, 1973). Because these plexopathies often cannot be attributed to crush injuries, vasculitis, or local infection, an autoimmune phenomenon has been suggested (Richter et al, 1973). Polyneuropathy and Guillain-Barre syndrome have been observed in several cases (Smith and Wilson, 1975; Richter et al, 1973). Muscle disorders, including acute rhabdomyolysis (Greenwood, 1974; Richter et al, 1971), chronic myopathy, and crush syndrome, are well-known consequences of heroin abuse, usually following overdose and coma. In most instances, these are presumed to be secondary to prolonged compression. However, IV injection of an adulterant may occasionally play a role in these cases.

Acute transverse myelitis, which may also present as a

Brown-Sequard syndrome (Krause, 1983) and usually occurs at the lower cervical and thoracic levels, may also occur with heroin abuse (Richter and Rosenberg, 1968; Richter et al, 1973). Pearson and Richter (1979) have reported an additional eight cases with this syndrome since the original report of four patients in 1968 (Richter and Rosenberg). There have been other instances of transverse myelitis reported as well (Lee et al, 1976; Ell et al, 1981). A variety of theories regarding the mechanism underlying the occurrence of tranverse myelitis in heroin addicts have been suggested, including compromised circulation to the cord, a hypersensitivity reaction involving the immune system (to heroin, quinine or other adulterants or possibly to hepatitis B antigen) and direct toxicity of heroin (Richter, 1984). Pathological examination of the cord in one case showed necrotic changes without evidence of vascular occlusion or embolic phenomenon (Richter et al, 1973).

Finally, it is worth noting that heroin addicts have been major targets of the recent synthetic revolution, particularly the fentanyl series, something which will be discussed later.

AMPHETAMINES

Racemic beta-phenylisopropylamine, known as amphetamine, was first synthesized in 1887 (Polson et al, 1983) and much later, in 1935, marketed clinically for the treatment of narcolepsy. Its psychological effects, which generally occur with an oral dose of 10 to 30 milligrams, include increased alertness, perceived physical well-being, increased confidence, anorexia, and improvement in the rapidity of mental processing and, sometimes, at higher doses, repetitive stereotypic behavior and mild paranoia. Amphetamine psychosis may occur after chronic abuse and bears resemblance to paranoid schizophrenia. Sudden death may occur from cardiac arrhythmias and, at high doses, seizures and hyperthermia may occur (Richter, 1984).

The pharmacological effects of amphetamine are predominantly mediated by the catecholaminergic systems in the CNS, where it appears to cause the release of neurotransmitters as well as blocking their re-uptake (Lewander, 1977). It is generally thought that the action of amphetamines with respect to alertness and anorexia is related to its effects on the noradrenergic system, while the stereotypic behavior seen in animals after amphetamine administration may be due to dopamine release (Lewander, 1977). Amphetamine associated vasculitis and intracerebral hemorrhage (ICH) have been repeatedly described in the literature (Citron et al, 1970; Olson, 1977; Salanova and Taubner, 1984; Edwards, 1977). After IV, nasal or oral use of amphetamine (Harrington et al, 1983) or related compounds (Wooten et al,1983), vasculitis may manifest with or without ICH (Bostwick, 1981), or ICH may occur without evidence of vasculitis (Delaney and Estes, 1980; D'Souza and Shraberg, 1981; Harrington et al, 1983). In fact, it has been suggested that a history of amphetamine abuse should be carefully searched for in any young adult presenting with unexplained intracranial lobar hematoma (Harrington et al, 1983).

Several hypotheses have been proposed to explain the induction of vasculitis and/or ICH by amphetamine. Because amphetamines are known to stimulate the heart, cause vasoconstriction and increase blood pressure, it has been suggested that sudden increases in blood pressure might cause ICH. One third of cases of ICH reported by Delany and Estes (1980) were admitted with increased blood pressure, and a particularly convincing case where increased blood pressure appeared to be the likely etiology has been reported by D'Souza and Shraberg (1981). Criticism of this hypothesis is that blood pressure may also be elevated secondary to an ICH, and many patients do not have elevated blood pressure when admitted. Hence, high blood pressure alone does not explain the ICH, at least in some patients. A second possibility is that the frequent physical injury and head trauma suffered by drug abusers predisposes them to ICH, but it is difficult to see how this accounts for those cases associated with vasculitis (Delaney and Estes, 1980). A third possibility is that there are many diluents in the street-obtained amphetamine, and that these adulterants could contribute to a cerebral vasculitis (Caplan et al, 1982). However, Harrington and colleagues (1983) have reported four patients who developed ICH while taking amphetamine-related compounds, one who took prescription drug orally which presumably represented pure compound. This latter patient, as well as one other, also had angiographic evidence of vasculitis, supporting the view that amphetamine itself causes the cerebral vascular changes (Harrington et al, 1983).

A fourth posssibility is that amphetamine vasculitis may directly or indirectly involve hepatitis B antigen (Koff et al,

1973) or other immunological mechanisms (Wooten et al, 1983). Certainly not all patients are positive for hepatitis B antigen, and this seems an unlikely unifying etiology. Additional immunologic mechanisms, on the other hand, have only been given preliminary attention and require further study.

Experimental evidence that amphetamine causes a vasculitis has been provided by Rumbaugh et al (1971). These investigators gave doses comparable to those used by drug abusers to rhesus monkeys and found a diffuse angiitis of major vessels on angiography and pathological evidence of a necrotizing vasculitis. However, Schuster and Fischman (1975) gave amphetamines to primates IV for 6 months, but were unable to demonstrate any vasculitis pathologically. Hence, the experimental evidence is conflicting, and we must conclude that the exact mechanism underlying this phenomenon has yet to be elucidated.

Dyskinesias (chorea and athetosis) represent one of the more intriguing complications of amphetamine abuse (Richter, 1984). They most often involve the facial and masticatory muscles (Goetz et al, 1981) and have interested investigators because they may shed some light on the pathophysiology of a variety of other disorders which are characterized by dyskinesia. The findings of Ricaurte and collegues (1984), that amphetamines may cause prolonged depletion of striatal dopamine, raise the possibility that dopamine receptor hypersensitivty may be involved in this phenomenon.

Two additional complications of methamphetamine abuse include mononeuropathy multiplex (Stafford et al, 1975) and acute subarachnoid hemorrhage (Chynn, 1975). The latter may have been secondary to vasculitis, although this has not been shown with certainty.

Death due to amphetamine overdose is very unusual and is generally due to some other drug or complication, in addition to amphetamine (Polson et al, 1983). However, a report of 10 cases with fatal amphetamine intoxication showed that CNS findings included petechial hemorrhages, subdural and subarachnoid hemorrhages and hydrocephalus (Zalis, 1963).

COCAINE

The leaves of *Erythroxylon coca*, which contain the alkaloid cocaine, have been consumed by natives in the Andes mountains for centuries. Sigmund Freud and Karl Koller were the first physicians to use cocaine clinically as a local anesthetic in 1884. It now appears to be undergoing a meteoric rise in popularity in the United States. Cocaine may be chewed (leaves, paste), taken intranasally (powder), smoked ("free basing"), or may be used intravenously either alone or in combination with heroin (known as a "speedball") or PCP ("sunshine"). Street names include coke, snow, gold dust and lady. It is rapidly metabolized by the liver, so is not effective orally.

Subjective effects include a sense of well-being and even euphoria. The user may experience a feeling of excitement and become loquacious and restless. At high dosages, difficulties with coordination, tremors, myoclonic jerks, and eventually generalized seizures may occur (Jeri et al, 1978). Cocaine psychosis is characterized by paranoia, marked agitation, hypervigilance, and hallucinations. At still higher dosages, depression of the CNS occurs and death from respiratory failure may follow. Death may also occur from cardiac arrhythmias and cardiac arrest (Jeri et al, 1978), hyperthermia, and acute hypertensive crises.

The pharmacological effects produced by cocaine are in many ways similar to amphetamine, and, in fact, the two drugs have a very similar history in terms of their use and abuse. Similar to amphetamine, the mechanism of action of cocaine appears to involve the potentiation of the catecholamine system by preventing neurotransmitter uptake (Jaffe, 1980).

Neurological complications of cocaine abuse, other than those related to overdose, are few. Those abusers who have come to our attention have been admitted to an inpatient psychiatric unit with a condition which can best be described as a combination of acute mania and paranoid schizophrenia. Because an atypical psychosis will occasionally lead to neurological consultation, it is in this context that such patients might be seen by the neurologist. Subarachnoid hemorrhage has been reported in two patients literally within minutes of snorting cocaine (Lichtenfeld et al, 1984). Sources of the bleeding were found in both (an aneurysm in one and arteriovenous malformation in the other), and it was suggested that a cocaine induced surge in blood pressure may have precipitated the hemorrhage. A right parietal lobe hemorrhage developed in another individual 30 minutes after snorting cocaine (Caplan et al, 1982). Cerebral infarction has also been reported in an individual who had used cocaine intramuscularly one to two hours earlier (Brust and and Richter, 1977).

PHENCYCLIDINE (PCP) AND THE LAUNCHING OF THE SYNTHETIC REVOLUTION

PCP was introduced in 1960 as a general anesthetic, but was soon discontinued because it also produced post-operative agitation and delirium. The drug reached maximum popularity in the illicit drug market in the 1960's, but developed a reputation for "bad trips" when taken orally. After the passage of the comprehensive Drug and Control Act of 1970, which banned LSD and certain other hallucinogenics altogether, PCP returned to popularity, and is once again widely available in the illicit drug market. Cases of intoxication have been reported in virtually all 50 states in the United States, and abuse has again reached epidemic proportions in some areas of the country.

One of the reasons for the popularity of PCP is that it is very easy and inexpencive to manufacture in a "kitchen laboratory." Further, users have discovered that the more severe side effects can be avoided by titrating intake, usually by smoking the compound until the desired effects are obtained. Common street names include angel dust, goon, hog, peace pills, and crystal. It was used as a veterinary anesthetic (Sernylan) until 1979, when all legal manufacture of the drug stopped. PCP is not a neurotoxin, but rather a potent pharmacologic agent, having both CNS depressant and stimulant effects, as well as hallucinogenic and anesthetic properties (Aniline and Pitts, 1982).

With small doses of PCP, a subjective sense of intoxication occurs. A staggering gait, slurred speech, nystagmus, and numbness of the extremities may all occur at this stage. Numbness of the extremities should be emphasized, as this symptom can provide an important clue to PCP intoxication in what may otherwise be a very confusing diagnostic situation. With increasing doses, hostile and bizarre behavior occur, and stupor and coma ensue as doses are further increased. However, the eyes often remain open, and such patients appear catatonic, similar to "akinetic mutes." On clinical examination, cardinal features include *nystagmus* and *hypertension*, which occur in 57% of patients (McCarron et al, 1981). Violence, bizarre behavior, and agitation are seen in 30-50% of patients. Cases of self-mutilation are well documented, and are probably due to the combination of its psychoactive effects combined with anesthesia. While lethargy, coma and confusional states are common, nearly half of intoxicated individuals will be alert and oriented.

Other neurological complications which may be encountered include major motor seizures, generalized rigidity, localized dystonias, catalepsy, and striking examples of chorea and athetosis (McCarron et al, 1981). Fatal intraventricular and subarachnoid hemorrhage has been reported in one patient (Bessen, 1982). Diagnosis may be difficult because individuals intoxicated with PCP may have peak blood levels of 50-200 ng/ml for periods of only 1-4 hours after an inhalation "hit" of 5-15 milligrams. As most laboratory tests are not sensitive below this level, determinations are often reported as non-detected. It is worth noting that detection in the urine is affected by pH, as excretion is greatly reduced when the urine is basic. With overdose, the half-life is about 3 days, but this can be shortened to 1 day with acidification of the urine (ammonium chloride is recommended), and continuous gastric suction (McCarron et al, 1981; Aniline and Pitts, 1982).

Chronic users report difficulties in memory, speech, and thinking, but these are poorly documented, and are said to clear in 6 to 12 months. Unusual aspects of PCP intoxication include abrupt lapses into bizarre confusional states hours and even days after clearing of the original behavioral disorder, and post-intoxication "schizophrenia-like" behavior for up to six weeks after acute intoxication (Aniline and Pitts, 1982). Whether or not some of these patients were already on their way to becoming schizophrenic remains a matter of debate. PCP has been shown to affect virtually every neurotransmitter system studied to date (Aniline and Pitts, 1982). Interestingly, it blocks re-uptake of dopamine (Johnson, 1983), suggesting this neurotransmitter might mediate some of the clinical effects of this compound. Valium has been recommended for treatment of convulsions if present. For control of psychotic behavior, haloperidol is recommended as phenothiazines may potentiate the anticholinergic actions of PCP (Burns and Lerner, 1976).

DESIGNER DRUGS AND MPTP

In the last few years, it has become apparent that a plethora of new products are brewing in the laboratories of our nation's illicit chemists. These have been referred to as "designer drugs" and were probably first observed in California. The term was originally coined to refer to the increasing ability of illicit chemists to design drugs tailored to meet an individual's personal specifications, including color, type of "high", potency, and duration of effect. We have broadened the definition of "designer drugs" to include a new and dangerous phenomenon whereby illicit chemists are now structurally redesigning well-known (and controlled) narcotics or stimulants in order to escape the law. PCP was the first drug to be modified in this way when thiophene was substituted for the phenyl ring. It is possible to alter and sell these drugs legally because current drug enforcement legislation in the United States requires that any controlled substance be designated specifically by name and structure, and these altered drugs have not been so designated. There are now at least 6 new "designer analogues" of the widely used general anesthetic fentanyl which have appeared in the illicit drug market in California in the last few years. Only one of these has been controlled to date (alpha-methyl-fentanyl). Some of these new compounds are estimated to be between 2000 to 7000 times more potent than morphine. Thus, the dose is difficult to titrate, and an estimated 40 to 50 deaths have occurred due to overdose in California alone.

Because there are obvious hazards to the above approach, a manufacturing and marketing explosion of this type in the illicit drug market is very alarming. First, these newly designed and tailored look-alikes are not tested in animals, but tried directly in humans (i.e., addicts) first. Hence, addicts injecting them are playing a form of Russian roulette, but using chemical bullets rather than lead ones (a phenomenon we have called "receptor roulette"). Second, there are no quality controls, and the risks of undesired by-products remains ever present. Third, as mentioned previously, many are so potent that the risk for overdose is greatly enhanced. Given this approach, it seemed inevitable that a true toxin would emerge sooner or later, and this is precisely what happened recently in northern California.

Sometime during 1981, an illicit chemist took a new approach to the designer drug phenomenon. Rather than slightly altering a well-known narcotic or psychoactive drug, this individual chose to research the literature until a previously synthesized narcotic was found which the government had failed to control. To do this, this chemist's search carried him back into the 1940s where he found a Demerol look-alike, known as 1-methyl-4-phenyl-4-propionoxy-piperidine (MPPP), which was described in a paper by Ziering and co-workers (1947). After carefully removing this article from the library (it was razor-bladed out, not checked out), the chemist apparently began synthesizing and wholesaling this compound in the illicit drug market in northern California as a "new synthetic heroin." However, during the Spring and Summer of 1982, heroin addicts purchasing this substance began to experience dramatic series of undesirable side effects (Langston et al, 1983a; Langston and Langston, 1983;

Ballard et al, 1984). Acutely, these included hallucinations, jerking of the extremities, visual blurring, seborrhea, difficulty opening the eyes, generalized tremors, and a peculiar burning sensation at the site of injection. However, the worst was yet to come. Within days to weeks of initiating usage of this substance, additional symptoms began to occur including marked slowness of movement, rigidity and stiffness, and in some cases, resting tremor. In a number of these patients, symptoms occurred on a delayed basis after cessation of drug use (days or even weeks later) and continued to evolve for up to two weeks. Examination of the most severely affected cases revealed rigidity, bradykinesia, masked facies, drooling, fixed stare, short-stepped shuffling gait (three were non-ambulatory), flexed posture, hypophonia and loss of postural righting reflexes. Perhaps even more remarkable was the fact that the remainder of the neurologic examination was completely normal. The six most severely affected patients were treated with L-dopa resulting in improvement of all symptoms. The single epidemiologic feature linking these individuals was the IV use of a new "synthetic" heroin. MPTP, which is a by-product in the synthesis of MPPP, proved to be the offending agent (Langston et al, 1983).

We now know that MPTP, when given systemically, is selectively toxic to the cells of the zona compacta of the substantia nigra in the rhesus monkey (Burns et al, 1983) and in the squirrel monkey (Langston et al, 1984a), thus creating an excellent animal model for Parkinson's disease. Careful examination of other portions of the central nervous system in animals exposed to this substance reveals no other evidence of neuropathological damage. Pathologic examination of a probable case of human exposure, which was actually reported several years earlier (although the offending agent was never specifically identified), revealed similar findings (Davis et al, 1979).

In the last year, research has focused on the mechanism of action of MPTP, as it is hoped that understanding why it is selectively toxic to the substantia nigra may shed light on the selective vulnerability of these cells in Parkinson's disease. It is now known that MPTP is rapidly converted to 1-methyl-4-phenylpyridinium ion or MPP+ (Chiba et al 1984, Langston et al 1984b; Markey 1984), and this conversion occurs in virtually every tissue studied to date except the eye (Langston et al, 1984b). Hence, the exact reason for the remarkable selectivity of MPTP for the substantia nigra is still unresolved.

One fascinating finding which has already emerged from the study of MPTP relates to monoamine oxidase. MAO appears to mediate the biotransformation of MPTP to MPP+, as MAO inhibitors block this conversion (Chiba et al 1984; Langston et al 1984c; Markey et al 1984) and neurotoxicity (Langston et al 1984c). This finding has accelerated interest in the possibility that MAO inhibitor therapy might actually slow the progression of idiopathic Parkinson's disease. Retrospective evidence that a selective MAO-B inhibitor (deprenyl) may slow the course of idiopathic Parkinson's disease has recently been reported by Birkmayer and colleagues (1983). It will be a remarkable irony if a compound produced in a "kitchen chemist's" illicit laboratory plays an important role in advancing our understanding of a major neurodegenerative disease of aging.

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[From the Congressional Record, Mar. 26, 1985]

S. 746

By Mr. CHILES:

S. 746. A bill to require the National Drug Enforcement Policy Board to provide a comprehensive assessment of the designer drug problem and make recommendations to Congress for necessary legislation; to the Committee on the Judiciary.

ASSESSMENT OF THE DESIGNER DRUG PROBLEM

Mr. CHILES. Mr. President, as one surveys the reality of drug abuse in this country and the constant flood of illegal narcotics that threatens the very fabric of our society, there doesn't seem to be room for any more bad news. Unfortunately, there is some new bad news; a developing problem that is left unaddressed and unresolved poses immense public health and law enforcement difficulties for the future. In the parlance of California, where this problem is emerging, they are called "designer drugs." One observer warns if they move to the rest of the country designer drugs, "may well topple America's 70-year policy of drug control and spark a public health disaster of overdose deaths, poisonings, and addiction." And in all likelihood they will spread to the rest of the country.

What is a designer drug? Originally it was a drug synthetically created by chemists and designed to fit the tastes of individual clients. Now it refers to a broader phenomenon of chemists modifying controlled substances to produce analogs or chemical cousins of these substances which are not convered by the Controlled Substances Act. By adding a fluoride or an extra carbon molecule, a new drug is created which will produce the high or euphoria the user seeks but is not illegal. Eventually DEA may move to control this new substance but the enterprising chemist will probably already be marketing some new variations. The purveyor of designer drugs can stay ahead of the law indefinitely.

The United States is devoting considerable resources and manpower to the effort to contain the flow of heroin, cocaine and marijuana. In light of the damage these narcotics inflict on our society and the crime they spawn, I think we should be doing more. However, whatever success we achieve in destroying drug crops and interdicting drug shipments will be of little consequence if the opium fields of Asia and the coca fields of Colombia are replaced by clandestine laboratories in the U.S.

At this point, designer drugs represent a small but growing factor in overall drug use. The chief of the California Division of Drug Programs projects that up to 20 percent of the State's heroin users are now taking some fentanyl analog to feed their habit. The more alarming facts are not the present statistics but the dangerous potential of these substances. These drugs can be made in small labs, with minimal materials and with readily available chemical formulas. A $500 investment in Chemicals can produce a $2 million batch of the synthetic heroin. In testimony before the President's Commission on Organized Crime it was estimated that a single chemist working an 8 hour day could, using the more potent fentanyl derivatives, supply the entire Nation's heroin demand on an on-going basis. Soon, if not already, organized crime will recognize that designer drugs represent an easy and immensely profitable means of supplying narcotics.

The disturbing nature of designer drugs is not simply that they are another source of illicit narcotics. Designer drugs pose additional and very troubling problems in terms of the public health consequences and our law enforcement response.

The more commonly used drugs—cocaine, marijuana and heroin—take a terrible toll on their users in health problems and even death. Designer drugs multiply these risks and open the door to long term neurodegenerative diseases, adding an entirely new dimension to the drug abuse problems. At least with the more traditional drugs there is some understanding of what physically happens to the user. Each batch of synthetic heroin or some other analog represents a chemical game of Russian roulette for the user. The fentanyl analogs, sold as heroin, are hundreds and even thousands of times more potent than morphine. Infinitesimal amounts of the drug can cause profound reactions. Already they have resulted in the deaths of 90 persons.

Beyond the great risk of overdose is the risk of incurring severe neurological impairment. No one knows what is in each batch of designer drugs. They are not tested; there is no process to remove contaminants or unwanted compounds; and the potential is very real that a highly toxic compound will hit the streets. In California a substance known as MPTP was circulated as "new heroin." It has caused severe brain damage similar to end-stage Parkinson's disease. California health authorities estimate that as many as 500 users of this substance may develop the symptoms of

Parkinson's disease. The human and medical economic costs of such an epidemic are almost incalculable. More recently, a designer drug user has been identified with the neurological symptoms of Huntington's chorea, a debilitating and eventually fatal disease.

All the signs indicate that designer drugs will be a major part of the drug abuse problem of the future. If that proves to be the case, the public health consequences of drug use may be entering an entirely new and frightening dimension.

Are we prepared to take action to stop this looming crisis? The answer is not encouraging. Synthetic narcotic analogs can be developed and produced faster than they can be identified and controlled. Even with the emergency scheduling provisions of the Controlled Substances Act, the clandestine labs can always stay beyond the reach of the law with a slightly different compound that is not yet on the schedule of controlled drugs. DEA could end up adding thousands and thousands of new entries to the list of illegal drugs with little impact on the availability of designer drugs.

DEA and other law enforcement agencies have experienced considerable problems in identifying synthetic narcotic analogs. They are very difficult to detect in drug samples or body fluids, as detection requires the most sensitive analytical techniques. Because of their exteme potency they are cut with large amounts of lactose or sucrose so the active drug present is very small, contributing nothing to the color, odor or taste of a sample. The fentanyl analogs are now available throughout much of California and since they are potent, difficult to detect and often legal, they could well become the drug of choice for heroin addicts. An anonymous addict interviewed on NBC news maintained, "I think heroin will gradually phase out as more and more illegal labs start to make the designer narcotics. It's definitely better as far as the rush and the high is concerned."

The current procedure for controlling illicit drugs, even with the emergency scheduling provisions authorized by Congress in 1984, represents an essentially unworkable response in the face of any significant increase in the manufacture of designer drugs. The Federal Register will simply be required reading for the criminal chemists to keept up to date on what analog formulas are now illegal and need to be modified.

Mr. President, our experience with illegal drug law enforcement is usually a matter of too little, too late. The problem reaches new levels of crisis while we search for the resources and tools to combat it. The potential disaster posed by the designer drug phenomenon is too grave for us to delay in finding means to prevent the manufacture and distribution of these drugs. It is apparent that present statute and policy will not do the job.

The National Narcotics Act of 1984 established the National Drug Enforcement Policy Board, chaired by the Attorney General, to coordinate and develop U.S. Government policy with respect to illegal drug law enforcement. I believe the Board must give priority attention to determining an effective strategy to control the spread of designer drugs. The Chairman is required to report to Congress on policy and planning for U.S. drug law enforcement. The initial report is due nine months after enactment. I am today introducing legislation requiring the Board to provide in that report to the Congress:

A comprehensive assessment of the current and potential contribution of synthetic narcotic analogs to the illegal narcotic problem in the United States;

Identification of illegal drug law enforcement strategies to prevent the manufacture and distribution of synthetic narcotic analogs;

Recommendations for necessary legislation.

I am also requesting the Office of Technology Assessment to initiate a workshop to examine the chemical, pharmacological, and regulatory questions involved in addressing the control of designer drugs so as to provide guidance to the Congress in the formulation of future legislation.

Mr. President, I believe the Congress must move expeditiously to address this problem but we must move with deliberation and an understanding of the difficult technical and pharmacological questions that need to be resolved in order to achieve an effective law enforcement policy. By requiring the National Drug Enforcement Policy Board to promptly address this issue and report to the Congress and by initiating an examination by the Office of Technology Assessment we will be laying the foundation for development of a responsible and workable policy.

99TH CONGRESS
1ST SESSION

S. 746

To require the National Drug Enforcement Policy Board to provide a comprehensive assessment of the designer drug problem and make recommendations to Congress for necessary legislation.

IN THE SENATE OF THE UNITED STATES

MARCH 26 (legislative day, FEBRUARY 18), 1985

Mr. CHILES introduced the following bill; which was read twice and referred to the Committee on the Judiciary

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A BILL

To require the National Drug Enforcement Policy Board to provide a comprehensive assessment of the designer drug problem and make recommendations to Congress for necessary legislation.

Be it enacted by the Senate and House of Representatives of the United States of America in Congress assembled, That (a) the Congress finds that—

(1) the use of illegal narcotics is a major health, law enforcement, and economic problem for the United States;

(2) the Congress has determined that the control of illegal narcotics and the prevention of drug abuse are national priorities;

(3) the Congress has identified "designer drugs" as new chemical analogs or variations of existing controlled substances, or other new substances, which have a psychedelic, stimulant, or depressant effect and have a high potential for abuse;

(4) these synthetic narcotic analogs are linked to numerous fatalities and incidence of severe neurodegenerative disease;

(5) significant increases in the consumption of synthetic narcotic analogs would pose an imminent hazard to the public safety;

(6) the virtually unlimited modification potential of synthetic narcotic analogs undermines effective implementation of the Controlled Substances Act;

(7) the National Narcotics Act of 1984 established the National Drug Enforcement Policy Board, designating the Attorney General as Chairman;

(8) the Board has among its responsibilities the development of United States policy with respect to illegal drug law enforcement; and

(9) the Chairman is required to report to the Congress on such policy by July of 1985.

(b) The purpose of this Act is to require the National Drug Enforcement Policy Board to provide a comprehensive assessment of the designer drug problem and make recommendations to Congress for necessary legislation.

SEC. 3. The initial report of the National Drug Enforcement Policy Board as required by section 1305 of the National Narcotics Act of 1984 (Chapter XIII, title II, Public Law 98-473) shall include—

(1) a comprehensive assessment of the current and potential contribution of synthetic narcotic analogs to the illegal narcotics problem in the United States;

(2) proposals for illegal drug law enforcement strategies to prevent the manufacture and distribution of synthetic narcotic analogs; and

(3) recommendations to the Congress for necessary legislation to eliminate the manufacture and distribution of illegal synthetic narcotic analogs.

AMENDED IN ASSEMBLY JUNE 24, 1985
AMENDED IN ASSEMBLY MAY 1, 1985
AMENDED IN ASSEMBLY APRIL 22, 1985

CALIFORNIA LEGISLATURE—1985–86 REGULAR SESSION

ASSEMBLY BILL No. 2401

Introduced by Assembly Member Filante

March 8, 1985

An act to amend Sections 11019, 11054, 11055, 11372.5, and 11488 of, to amend and renumber the headings of Article 4 (commencing with Section 11240), Article 5 (commencing with Section 11250), and Article 6 (commencing with Section 11260) of, Chapter 5 of Division 10 of, and to repeal Article 3 (commencing with Section 11230) of, the Health and Safety Code, and to amend Section 1203.07 of the Penal Code, relating to controlled substances, *and declaring the urgency thereof, to take effect immediately*.

LEGISLATIVE COUNSEL'S DIGEST

AB 2401, as amended, Filante. Controlled substances.

(1) Existing law defines "narcotic drug" for purposes of the California Uniform Controlled Substances Act. That definition does not include acetylfentanyl or acetylthiofentanyl.

This bill would include those substances and their derivatives, salts, compounds, isomers, and preparations in that definition.

(2) Existing law specifies the substances that are included in Schedules I and II of controlled substances.

This bill would delete alpha-methylfentanyl from Schedule I and include derivatives of acetylfentanyl and acetylthiofentanyl in Schedule II, and would make other corrective changes in those schedules.

The bill would create a state-mandated local program by changing the definition of a crime.

(3) Existing law requires a physician prescribing or furnishing a controlled substance classified in Schedule II to an habitual user to furnish a report containing specified information to the Attorney General plus any additional reports requested by the Attorney General regarding the treatment of the user.

This bill would repeal these provisions. The bill would also make conforming technical, nonsubstantive changes.

(4) Existing law requires every person who is convicted of specified controlled substance offenses to pay an additional $50 fine imposed as a criminal laboratory analysis fee, and authorizes a peace officer making or attempting to make an arrest for specified controlled substances offenses to seize various property which is subject to forfeiture.

This bill would include additional specified offenses relating to the manufacture of controlled substances within those provisions.

Existing law prohibits the granting of probation or suspension of the execution or imposition of the sentence for persons convicted of manufacturing phencyclidine, but not for offering to manufacture phencyclidine.

This bill would include convictions of offering to perform specified acts relating to the manufacture of phencyclidine in that prohibition.

(5) The California Constitution requires the state to reimburse local agencies and school districts for certain costs mandated by the state. Statutory provisions establish procedures for making that reimbursement.

This bill would provide that no reimbursement is required by this act for a specified reason.

(6) The bill would take effect immediately as an urgency statute.

Vote: ~~majority~~ ⅔. Appropriation: no. Fiscal committee: yes. State-mandated local program: yes.

The people of the State of California do enact as follows:

SECTION 1. Section 11019 of the Health and Safety Code is amended to read:

11019. "Narcotic drug" means any of the following, whether produced directly or indirectly by extraction from substances of vegetable origin, or independently by means of chemical synthesis, or by a combination of extraction and chemical synthesis:

(a) Opium and opiate, and any salt, compound, derivative, or preparation of opium or opiate.

(b) Any salt, compound, isomer, or derivative, whether natural or synthetic, of the substances referred to in subdivision (a), but not including the isoquinoline alkaloids of opium.

(c) Opium poppy and poppy straw.

(d) Coca leaves and any salt, compound, derivative, or preparation of coca leaves, but not including decocainized coca leaves or extractions of coca leaves which do not contain cocaine or ecgonine.

(e) Cocaine, whether natural or synthetic, or any salt, isomer, derivative, or preparation thereof.

(f) Ecgonine, whether natural or synthetic, or any salt, isomer, derivative, or preparation thereof.

(g) Acetylfentanyl and any derivative, salt, compound, isomer, or preparation of acetylfentanyl.

(h) Acetylthiofentanyl and any derivative, salt, compound, isomer, or preparation of acetylthiofentanyl.

SEC. 1.2. Section 11054 of the Health and Safety Code is amended to read:

11054. (a) The controlled substances listed in this section are included in Schedule I.

(b) Opiates. Unless specifically excepted or unless listed in another schedule, any of the following opiates, including their isomers, esters, ethers, salts, and salts of isomers, esters, and ethers whenever the existence of those isomers, esters, ethers, and salts is possible within the specific chemical designation:

(1) Acetylmethadol.

(2) Allylprodine.

(3) Alphacetylmethadol.
(4) Alphameprodine.
(5) Alphamethadol.
(6) Benzethidine.
(7) Betacetylmethadol.
(8) Betameprodine.
(9) Betamethadol.
(10) Betaprodine.
(11) Clonitazene.
(12) Dextromoramide.
(13) Diampromide.
(14) Diethylthiambutene.
(15) Difenoxin.
(16) Dimenoxadol.
(17) Dimepheptanol.
(18) Dimethylthiambutene.
(19) Dioxaphetyl butyrate.
(20) Dipipanone.
(21) Ethylmethylthiambutene.
(22) Etonitazene.
(23) Etoxeridine.
(24) Furethidine.
(25) Hydroxypethidine.
(26) Ketobemidone.
(27) Levomoramide.
(28) Levophenacylmorphan.
(29) Morpheridine.
(30) Noracymethadol.
(31) Norlevorphanol.
(32) Normethadone.
(33) Norpipanone.
(34) Phenadoxone.
(35) Phenampromide.
(36) Phenomorphan.
(37) Phenoperidine.
(38) Piritramide.
(39) Proheptazine.
(40) Properidine.
(41) Propiram.
(42) Racemoramide.

(43) Tilidine.
(44) Trimeperidine.

(c) Opium derivatives. Unless specifically excepted or unless listed in another schedule, any of the following opium derivatives, its salts, isomers, and salts of isomers whenever the existence of those salts, isomers, and salts of isomers is possible within the specific chemical designation:

(1) Acetorphine.
(2) Acetyldihydrocodeine.
(3) Benzylmorphine.
(4) Codeine methylbromide.
(5) Codeine-N-Oxide.
(6) Cyprenorphine.
(7) Desomorphine.
(8) Dihydromorphine.
(9) Drotebanol.
(10) Etorphine (except hydrochloride salt)
(11) Heroin.
(12) Hydromorphinol.
(13) Methyldesorphine.
(14) Methyldihydromorphine.
(15) Morphine methylbromide.
(16) Morphine methylsulfonate.
(17) Morphine-N-Oxide.
(18) Myrophine.
(19) Nicocodeine.
(20) Nicomorphine.
(21) Normorphine.
(22) Pholcodine.
(23) Thebacon.

(d) Hallucinogenic substances. Unless specifically excepted or unless listed in another schedule, any material, compound, mixture, or preparation, which contains any quantity of the following hallucinogenic substances, or which contains any of its salts, isomers, and salts of isomers whenever the existence of those salts, isomers, and salts of isomers is possible within the specific chemical designation (for purposes of this subdivision only, the term "isomer" includes the optical, position, and geometric isomers):

(1) 4-bromo-2,5 dimethoxy-amphetamine — Some trade or other names: 4-bromo-2,5-dimethoxy-alpha-methylphenethylamine; 4-bromo-2,5-DMA.

(2) 2,5-dimethoxyamphetamine — Some trade or other names: 2,5-dimethoxy-alpha-methylphenethylamine; 2,5-DMA.

(3) 4-methoxyamphetamine — Some trade or other names: 4-methoxy-alpha-methylphenethylamine, paramethoxyamphetamine, PMA.

(4) 5-methoxy-3,4-methylenedioxy-amphetamine.

(5) 4-methyl-2,5-dimethoxy-amphetamine — Some trade or other names: 4-methyl-2,5 dimethoxy-alpha-methylphenethylamine; “DOM”; and “STP”.

(6) 3, 4-methylenedioxy amphetamine.

(7) 3,4,5-trimethoxy amphetamine.

(8) Bufotenine — Some trade or other names: 3-(beta-Dimethylaminoethyl)-5-hydroxyindole; 3-(2-dimethylaminoethyl)-5 indolol; N,N-dimethylserolonin, 5-hydroxy-N,N-dimethyltryptamine; mappine.

(9) Diethyltrypatamine — Some trade or other names: N,N-Diethyltryptamine; DET.

(10) Dimethyltryptamine — Some trade or other names: DMT.

(11) Ibogaine — Some trade or other names: 7-Ethyl-6,6beta, 7,8,9,10,12,13-octahydro-2-methoxy-6,9-methano-5H-pyrido [1',2':1,2] azepino [5,4-b] indole; Tabernanthe iboga.

(12) Lysergic acid diethylamide.

(13) Marijuana.

(14) Mescaline.

(15) Peyote — Meaning all parts of the plant presently classified botanically as Lophophora williamsii Lemaire, whether growing or not, the seeds thereof, any extract from any part of such plant, and every compound, manufacture, salts, derivative, mixture, or preparation of such plant, its seeds or extracts (interprets 21 U.S.C. Sec. 812(c), Schedule 1(c) (12)).

(16) N-ethyl-3-piperidyl benzilate.

(17) N-methyl-3-piperidyl benzilate.

(18) Psilocybin.

(19) Psilocyn.

(20) Tetrahydrocannabinols. Synthetic equivalents of the substances contained in the plant, or in the resinous extractives of Cannabis, sp. and/or synthetic substances, derivatives, and their isomers with similar chemical structure and pharmacological activity such as the following: delta 1 cis or trans tetrahydrocannabinol, and their optical isomers; delta 6 cis or trans tetrahydrocannabinol, and their optical isomers; delta 3,4 cis or trans tetrahydrocannabinol, and its optical isomers.

(Since nomenclature of these substances is not internationally standardized, compounds of these structures, regardless of numerical designation of atomic positions covered).

(21) Ethylamine analog of phencyclidine — Some trade or other names: N-ethyl-1-phenylcyclohexylamine, (1-phenylcyclohexyl) ethylamine, N-(1-phenylcyclohexyl) ethylamine, cyclohexamine, PCE.

(22) Pyrrolidine analog of phencyclidine — Some trade or other names: 1-(1-phenylcyclohexyl)-pyrrolidine, PCPy, PHP.

(23) Thiophene analog of phencyclidine — Some trade or other names: 1-[1-(2 thienyl)-cyclohexyl]-piperidine, 2-thienyl analog of phencyclidine, TPCP, TCP.

(e) Depressants. Unless specifically excepted or unless listed in another schedule, any material, compound, mixture, or preparation which contains any quantity of the following substances having a depressant effect on the central nervous system, including its salts, isomers, and salts of isomers whenever the existence of those salts, isomers, and salts of isomers is possible within the specific chemical designation:

(1) Mecloqualone.

(2) Methaqualone.

SEC. 1.4. Section 11055 of the Health and Safety Code is amended to read:

11055. (a) The controlled substances listed in this section are included in Schedule II.

(b) Any of the following substances, except those narcotic drugs listed in other schedules, whether produced directly or indirectly by extraction from substances of vegetable origin, or independently by means of chemical synthesis, or by combination of extraction and chemical synthesis:

(1) Opium and opiate, and any salt, compound, derivative, or preparation of opium or opiate, with the exception of naloxone hydrochloride (N-allyl-14-hydroxy-nordihydromorphinone hydrochloride), but including the following:

(A) Raw opium.

(B) Opium extracts.

(C) Opium fluid extracts.

(D) Powdered opium.

(E) Granulated opium.

(F) Tincture of opium.

(G) Apomorphine.

(H) Codeine.

(I) Ethylmorphine.

(J) Hydrocodone.

(K) Hydromorphone.

(L) Metopon.

(M) Morphine.

(N) Oxycodone.

(O) Oxymorphone.

(P) Thebaine.

(2) Any salt, compound, isomer, or derivative, whether natural or synthetic, of the substances referred to in paragraph (1), but not including the isoquinoline alkaloids of opium.

(3) Opium poppy and poppy straw.

(4) Coca leaves and any salt, compound, derivative, or preparation of coca leaves, but not including decocainized coca leaves or extractions which do not contain cocaine or ecgonine.

(5) Concentrate of poppy straw (the crude extract of

poppy straw in either liquid, solid, or powder form which contains the phenanthrene alkaloids of the opium poppy).

(6) Cocaine, whether natural or synthetic, or any salt, isomer, derivative, or preparation thereof.

(7) Ecgonine, whether natural or synthetic, or any salt, isomer, derivative, or preparation thereof.

(c) Opiates. Unless specifically excepted or unless in another schedule, any of the following opiates, including its isomers, esters, ethers, salts, and salts of isomers, esters, and ethers whenever the existence of those isomers, esters, ethers, and salts is possible within the specific chemical designation, dextrorphan and levopropoxyphene excepted:

(1) Alphaprodine.

(2) Anileridine.

(3) Bezitramide.

(4) Bulk dextropropoxyphene (nondosage forms).

(5) Dihydrocodeine.

(6) Diphenoxylate.

(7) Fentanyl.

(8) Any substance which contains any quantity of a derivative of acetylfentanyl (N-[1-phenethyl-4-piperidyl] acetanilide), or any salt, compound, isomer, or preparation of a derivative of acetylfentanyl.

(9) Any substance which contains any quantity of a derivative of acetylthiofentanyl (N-[1-[2-(2-thienyl)enthyl]-4-peperidyl] acetanilide) or any salt, compound, isomer, or preparation of a derivative of acetylthiofentanyl.

(10) Isomethadone.

(11) Levomethorphan.

(12) Levorphanol.

(13) Metazocine.

(14) Methadone.

(15) Methadone-Intermediate, 4-cyano-2-dimethylamino-4, 4-diphenyl butane.

(16) Moramide-Intermediate, 2-methyl-3-morpholino-1, 1-diphenylpropane-carboxylic acid.

(17) Pethidine (meperidine).

(18) Pethidine-Intermediate-A, 4-cyano-1-methyl-4-phenylpiperidine.

(19) Pethidine-Intermediate-B, ethyl-4-phenylpiperidine-4-carboxylate.

(20) Pethidine-Intermediate-C,-1-methyl 4-phenylpiperidine-4-carboxylic acid.

(21) Phenazocine.

(22) Piminodine.

(23) Racemethorphan.

(24) Racemorphan.

(d) Stimulants. Unless specifically excepted or unless listed in another schedule, any material, compound, mixture, or preparation which contains any quantity of the following substances having a stimulant effect on the central nervous system:

(1) Amphetamine, its salts, optical isomers, and salts of its optical isomers.

(2) Methamphetamine, its salts, isomers, and salts of its isomers.

(3) Phenmetrazine and its salts.

(4) Methylphenidate.

(e) Depressants. Unless specifically excepted or unless listed in another schedule, any material, compound, mixture, or preparation which contains any quantity of the following substances having a depressant effect on the central nervous system, including its salts, isomers, and salts of isomers whenever the existence of those salts, isomers, and salts of isomers is possible within the specific chemical designation:

(1) Amobarbital.

(2) Pentobarbital.

(3) Phencyclidines, including the following:

(A) 1-(1-phenylcyclohexyl) piperidine (PCP).

(B) 1-(1-phenylcyclohexyl) morpholine (PCM).

The Attorney General, or his or her designee, may, by rule or regulation, add additional analogs of phencyclidine to those enumerated in this paragraph after notice, posting, and hearing pursuant to Chapter 3.5 (commencing with Section 11340) of Part 1 of Division 3 of Title 2 of the Government Code. The Attorney

General shall, in the calendar year of the regular session of the Legislature in which the rule or regulation is adopted, submit a draft of a proposed bill to each house of the Legislature which would incorporate the analogs into this code. No rule or regulation shall remain in effect beyond January 1 after the calendar year of the regular session in which the draft of the proposed bill is submitted to each house. However, if the draft of the proposed bill is submitted during a recess of the Legislature exceeding 45 calendar days, the rule or regulation shall be effective until January 1 after the next calendar year.

(4) Secobarbital.

(f) Immediate precursors. Unless specifically excepted or unless listed in another schedule, any material, compound, mixture, or preparation which contains any quantity of the following substances:

(1) Immediate precursor to amphetamine and methamphetamine:

(A) Phenylacetone. Some trade or other names: phenyl-2 propanone; P2P; benzyl methyl ketone; methyl benzyl ketone.

(2) Immediate precursors to phencyclidine (PCP):

(A) 1-phenylcyclohexylamine.

(B) 1-piperidinocyclohexanecarbonitrile (PCC).

SEC. 1.5. Article 3 (commencing with Section 11230) of Chapter 5 of Division 10 of the Health and Safety Code is repealed.

SEC. 2. The heading of Article 4 (commencing with Section 11240) of Chapter 5 of Division 10 of the Health and Safety Code is amended and renumbered to read:

Article 3. Veterinarians

SEC. 3. The heading of Article 5 (commencing with Section 11250) of Chapter 5 of Division 10 of the Health and Safety Code is amended and renumbered to read:

Article 4. Sale Without Prescription

SEC. 4. The heading of Article 6 (commencing with Section 11260) of Chapter 5 of Division 10 of the Health and Safety Code is amended and renumbered to read:

Article 5. Cannabis Therapeutic Research Program

SEC. 5. Section 11372.5 of the Health and Safety Code is amended to read:

11372.5. (a) Every person who is convicted of a violation of Section 11350, 11351, 11352, 11355, 11358, 11359, 11361, 11363, 11364, 11368, 11377, 11378, 11378.5, 11379, 11379.5, 11379.6, 11380, 11380.5, 11382, 11383, or 11550 or subdivision (a) or (c) of Section 11357, or subdivision (a) of Section 11360 shall pay a criminal laboratory analysis fee in the amount of fifty dollars ($50) for each separate offense. The court shall increase the total fine necessary to include this increment.

With respect to those offenses specified in this subdivision for which a fine is not authorized by other provisions of law, the court may, upon conviction, impose a fine in an amount not to exceed fifty dollars ($50), which shall constitute the increment prescribed by this section and which shall be in addition to any other penalty prescribed by law.

(b) The county treasurer shall maintain a criminalistics laboratories fund. The sum of fifty dollars ($50) shall be deposited into the fund for every conviction under Sections 11350, 11351, 11352, 11355, 11358, 11359, 11361, 11363, 11364, 11368, 11377, 11378, 11378.5, 11379, 11379.5, 11379.6, 11380, 11380.5, 11382, 11383, or 11550, subdivision (a) or (c) of Section 11357, or subdivision (a) of Section 11360, in addition to fines, forfeitures, and other moneys which are transmitted by the courts to the county treasurer pursuant to Section 11502. Such deposits shall be made prior to any transfer pursuant to Section 11502. The county may retain an amount of such money equal to its administrative cost incurred pursuant to this section. Moneys in the criminalistics laboratories fund shall, except as otherwise provided in this section, be used exclusively to fund (1) costs incurred by criminalistics laboratories providing microscopic and chemical analyses for controlled substances, in connection with criminal investigations conducted within both the incorporated or unincorporated portions of the county, (2) the purchase and maintenance of equipment for use by these laboratories in performing such analyses, and (3) for continuing education, training, and scientific development of forensic scientists regularly employed by these laboratories. Moneys in the criminalistics laboratory fund shall be in addition to any allocations pursuant to existing law. As used in this section, "criminalistics laboratory" means a laboratory operated by, or under contract with, a city, county, or other public agency, including a criminalistics laboratory of the Department of Justice, (1) which has not less than one regularly employed forensic scientist engaged in the analysis of solid-dose controlled substances, and (2) which is registered as an analytical laboratory with the Drug Enforcement Administration of the United States Department of Justice for the possession of all scheduled controlled substances. In counties served by criminalistics laboratories of the Department of Justice, amounts deposited in the criminalistics laboratories fund, after deduction of appropriate and reasonable county overhead charges attributable to the collection thereof, shall be paid by the county treasurer once a month to the Controller for deposit into the State General Fund, and shall be excepted from the expenditure requirements otherwise prescribed by this subdivision.

The county treasurer shall, at the conclusion of each fiscal year, determine the amount of any funds remaining in the special fund established pursuant to this section after expenditures for that fiscal year have been made for the purposes herein specified. The county treasurer shall annually distribute such surplus funds in accordance with the allocation scheme for distribution of fines and forfeitures set forth in Section 11502.

SEC. 6. Section 11488 of the Health and Safety Code is amended to read:

11488. (a) Any peace officer of this state, subsequent to making or attempting to make an arrest for a violation of Section 11351, 11352, 11355, 11359, 11360, 11378, 11378.5, 11379, 11379.5, 11379.6, or 11382 of this code, or Section 182 of the Penal Code insofar as the offense involves manufacture, sale, possession for sale or offer to manufacture or sell, or conspiracy to commit one of those offenses, may seize all moneys, negotiable instruments, securities, boats, vehicles, airplanes, or other things of value which the officer has probable cause to believe are forfeitable pursuant to subdivision (e) or (f) of Section 11470.

(b) The peace officer shall notify the Franchise Tax Board of a seizure where there is reasonable cause to believe that the value of the seized property exceeds five thousand dollars ($5,000).

(c) Receipts for property seized pursuant to this section shall be delivered to any person out of whose possession such property was seized, in accordance with Section 1412 of the Penal Code. In the event property seized was not seized out of anyone's possession, receipt for the property shall be delivered to the individual in possession of the premises at which the property was seized.

(d) There shall be a presumption affecting the burden of proof that the person to whom a receipt for property was issued is the owner thereof. This presumption may, however, be rebutted at the forfeiture hearing specified in Section 11488.5.

SEC. 7. Section 1203.07 of the Penal Code is amended to read:

1203.07. (a) Notwithstanding Section 1203, probation shall not be granted to, nor shall the execution or imposition of sentence be suspended for, any of the following persons:

(1) Any person who is convicted of violating Section 11351 of the Health and Safety Code by possessing for sale 14.25 grams or more of a substance containing heroin.

(2) Any person who is convicted of violating Section 11352 of the Health and Safety Code by selling or offering to sell 14.25 grams or more of a substance containing heroin.

(3) Any person convicted of violating Section 11351 of the Health and Safety Code by possessing heroin for sale or convicted of violating Section 11352 of the Health and Safety Code by selling or offering to sell heroin, and who has one or more prior convictions for violating Section 11351 or Section 11352 of the Health and Safety Code.

(4) Any person who is convicted of violating Section 11378.5 of the Health and Safety Code by possessing for sale 14.25 grams or more of any salt or solution of any controlled substance specified in paragraph (21), (22), or (23) of subdivision (d) of Section 11054 or in paragraph (3) of subdivision (e) of Section 11055 of the Health and Safety Code.

(5) Any person who is convicted of violating Section 11379.5 of the Health and Safety Code by transporting for sale, importing for sale, or administering phencyclidine, or offering to transport for sale, import for sale, or administer phencyclidine, or by attempting to import for sale or transport for sale phencyclidine.

(6) Any person who is convicted of violating Section 11379.5 of the Health and Safety Code by selling, or offering to sell phencyclidine.

(7) Any person who is convicted of violating Section 11379.6 of the Health and Safety Code by manufacturing phencyclidine or offering to perform an act involving the manufacture of phencyclidine in violation of subdivision (b) of Section 11379.6.

As used in this section "manufacture" refers to the act of any person who manufactures, compounds, converts, produces, derives, processes, or prepares, either directly or indirectly by chemical extraction or independently by means of chemical synthesis.

(8) Any person who is convicted of violating Section 11380.5 of the Health and Safety Code by the use of a minor as an agent or who solicits, induces, encourages, or intimidates a minor with the intent that the minor shall

violate the provisions of Section 11378.5, 11379.5, or 11379.6 of the Health and Safety Code insofar as the violation relates to phencyclidine or any of its analogs as specified in paragraph (21), (22), or (23) of subdivision (d) of Section 11054 or paragraph (3) of subdivision (e) of Section 11055 of the Health and Safety Code.

(9) Any person who is convicted of violating subdivision (b) of Section 11383 of the Health and Safety Code by possessing piperidine and cyclohexanone with intent to manufacture phencyclidine.

(b) The existence of any fact which would make a person ineligible for probation under subdivision (a) shall be alleged in the information or indictment, and either admitted by the defendant in open court, or found to be true by the jury trying the issue of guilt or by the court where guilt is established by plea of guilty or nolo contendere or by trial by the court sitting without a jury.

SEC. 8. The Legislature finds and declares that one purpose of this act is to include the various derivatives of actylfentanyl in controlled substance schedules. The Legislature further finds and declares that this act is intended to cover the "designer drugs" which are not presently covered by the Uniform Controlled Substances Act and which have caused serious injury and multiple deaths in California in the last several years. This act is intended to include actylfentanyl and its derivatives including sufentanil and alpha-methylfentanyl in Schedule II of the Uniform Controlled Substances Act and thereby to subject additional variants of actylfentanyl to prescription requirements and criminal penalties for violations of various provisions of the Health and Safety Code including those relating to sale and manufacture. The Legislature further expressly finds and declares that nothing in this act is intended to reduce or eliminate any penalties or prohibitions currently prescribed as to any controlled substances.

SEC. 9. No reimbursement is required by this act pursuant to Section 6 of Article XIII B of the California Constitution because the only costs which may be incurred by a local agency or school district will be incurred because this act creates a new crime or infraction, changes the definition of a crime or infraction, changes the penalty for a crime or infraction, or eliminates a crime or infraction.

SEC. 10. This act is an urgency statute necessary for the immediate preservation of the public peace, health, or safety within the meaning of Article IV of the Constitution and shall go into immediate effect. The facts constituting the necessity are:

Because the availability of designer drugs constitutes a serious threat to the health and safety of the people of California, it is necessary that this act take effect immediately.

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RECORD # 40 RF: RN 85 017282 PAGE NO. 1
Substantive

AMENDMENTS TO ASSEMBLY BILL NO. 2401
AS AMENDED IN ASSEMBLY JUNE 24, 1985

Amendment 1

In line 1 of the title, after "11055," insert:

11058,

Amendment 2

On page 3, strike out lines 23 to 26, inclusive, and insert:

(g) Acetylfentanyl, the thiophene analog thereof, derivatives of either, and any salt, compound, isomer, or preparation of acetylfentanyl or the thiophene analog thereof.

Amendment 3

On page 5, between lines 2 and 3, insert:

(45) Any substance which contains any quantity of acetylfentanyl (N-[1-phenethyl-4-piperidinyl] acetanilide) or a derivative thereof.

(46) Any substance which contains any quantity of the thiophene analog of acetylfentanyl (N-[1-[2-(2-thienyl)ethyl]-4-piperidinyl] acetanilide) or a derivative thereof.

Amendment 4

On page 5, line 15, strike out "Alphaprodine" and insert:

Alfentanyl

Amendment 5

On page 9, line 16, strike out "Anileridine" and insert:

Alphaprodine

Amendment 6

On page 9, line 17, strike out "Bezitramide" and insert:

Anileridine

Amendment 7

On page 9, line 18, strike out "Bulk dextropropoxyphene (nondosage forms)" and insert:

Bezitramide

Amendment 8

On page 9, line 19, strike out "Dihydrocodeine" and insert:

Bulk dextropropoxyphene (nondosage forms)

Amendment 9

On page 9, line 20, strike out "Diphenoxylate" and insert:

Dihydrocodeine

Amendment 10

On page 9, line 21, strike out "Fentanyl" and insert:

Diphenoxylate

Amendment 11-12

On page 9, strike out lines 22 to 30, inclusive, and insert:

(8) Fentanyl.

Amendment 13

On page 9, line 31, strike out "(10)" and insert:

(9)

Amendment 14

On page 9, line 32, strike out "(11)" and insert:

(10)

Amendment 15

On page 9, line 33, strike out "(12)" and insert:

(11)

Amendment 16

On page 9, line 34, strike out "(13)" and
insert:

(12)

Amendment 17
On page 9, line 35, strike out "(14)" and
insert:

(13)

Amendment 18
On page 9, line 36, strike out "(15)" and
insert:

(14)

Amendment 19
On page 9, line 38, strike out "(16)" and
insert:

(15)

Amendment 20
On page 9, line 40, strike out "(17)" and
insert:

(16)

Amendment 21
On page 10, line 1, strike out "(18)" and
insert:

(17)

Amendment 22
On page 10, line 3, strike out "(19)" and
insert:

(18)

Amendment 23
On page 10, line 5, strike out "(20)" and
insert:

(19)

Amendment 24

On page 10, line 7, strike out "(21)" and insert:

(20)

Amendment 25

On page 10, line 8, strike out "(22)" and insert:

(21)

Amendment 26

On page 10, line 9, strike out "(23)" and insert:

(22)

Amendment 27

On page 10, line 10, strike out "(24)" and insert:

(23)

Amendment 28

On page 10, between lines 10 and 11, insert:

(24) Sufentanyl

Amendment 29

On page 11, line 24, strike out "1-piperidinocyclohexanecarbonitrile" and insert:

1-piperidinocyclohexane Carbonitrile

Amendment 30

On page 11, between lines 24 and 25, insert:

SEC. 1.2. Section 11058 of the Health and Safety Code is amended to read:

11058. (a) The controlled substances listed in this section are included in Schedule V.

(b) Schedule V shall consist of the drugs and other substances, by whatever official name, common or usual name, chemical name, or brand name designated, listed in this section.

(c) Narcotic drugs containing nonnarcotic active medicinal ingredients. Any compound, mixture, or preparation containing any of the following narcotic drugs, or their salts calculated as the free anhydrous base or alkaloid, in limited quantities as set forth below, which shall include one or more nonnarcotic active medicinal ingredients in sufficient proportion to confer upon the compound, mixture, or preparation valuable medicinal qualities other than those possessed by narcotic drugs alone:

(1) Not more than 200 milligrams of codeine per 100 milliliters or per 100 grams.

(2) Not more than 100 milligrams of dihydrocodeine per 100 milliliters or per 100 grams.

(3) Not more than 100 milligrams of ethylmorphine per 100 milliliters or per 100 grams.

(4) Not more than 2.5 milligrams of diphenoxylate and not less than 25 micrograms of atropine sulfate per dosage unit.

(5) Not more than 100 milligrams of opium per 100 milliliters or per 100 grams.

(6) Not more than 0.5 milligram of difenoxin and not less than 25 micrograms of atropine sulfate per dosage unit.

(d) Loperamide.

(e) Buprenorphine.

Amendment 31

On page 16, strike out line 22 and insert:

intended to cover certain synthetic drugs which are not

99TH CONGRESS
1ST SESSION

S. 1437

To amend the Controlled Substances Act to create new penalties for the manufacturing with intent to distribute, the possession with intent to distribute, or the distribution of "designer drugs", and for other purposes.

IN THE SENATE OF THE UNITED STATES

JULY 16, 1985

Mr. THURMOND (for himself, Mrs. HAWKINS, Mr. CHILES, Mr. BIDEN, Mr. DECONCINI, Mr. SIMPSON, Mr. COCHRAN, Mr. MURKOWSKI, and Mr. SPECTER) introduced the following bill; which was read twice and referred to the Committee on the Judiciary

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A BILL

To amend the Controlled Substances Act to create new penalties for the manufacturing with intent to distribute, the possession with intent to distribute, or the distribution of "designer drugs", and for other purposes.

Be it enacted by the Senate and House of Representatives of the United States of America in Congress assembled, That this Act may be cited as the " 'Designer Drug' Enforcement Act of 1985".

SEC. 2. Part D of the Controlled Substances Act is amended by adding after section 403 the following new section 403A (21 U.S.C. 843):

"§ 403A. Prohibited acts D

"Any person who knowingly or internationally manufactures with intent to distribute, possesses with intent to distribute, or distributes a designer drug intended for human consumption shall be fined not more than $250,000, or imprisoned not more than fifteen years, or both. This section does not apply to a person who manufactures or distributes a substance in conformance with the provisions of an approved new drug application or an exemption for investigational use within the meaning of section 505 of the Federal Food, Drug, and Cosmetic Act (21 U.S.C. 355). For purposes of this section, section 505 of the Federal Food, Drug, and Cosmetic Act (21 U.S.C. 355) shall be applicable to the introduction or delivery for introduction of any new drug into intrastate, interstate, or foreign commerce.".

SEC. 3. Section 102 of the Controlled Substances Act (21 U.S.C. 802) is amended by adding at the end thereof the following new paragraphs:

"(31) The term 'designer drug' as used in section 403A means a substance other than a controlled substance that has a chemical structure substantially similar to that of a controlled substance in schedules I or II or that was specifically designed to produce an effect substantially similar to that of a controlled substance in schedules I or II. Examples of chemical classes in which designer drugs are found include, but are not limited to, the following: phenethylamines, N-substituted piperidines, morphinans, ecogonines, quinazolinones, substituted indoles, and arylcycloalkylamines.

"(32) The term 'human consumption' includes application, injection, inhalation, or ingestion.".

SEC. 4. The analysis of part D of the Controlled Substances Act is amended by inserting after the item relating to section 403 the following:

"403A. Prohibited acts D.".

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